**Exclusive breastfeeding and cognition, executive function and behavioural disorders in primary school-aged children in rural South Africa: a cohort analysis**

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**Running title:** Factors associated with child development

**Abstract**

**Background**

Exclusive breastfeeding (EBF) is associated with early child health; longer-term benefits for child development remain inconclusive. We examine associations between EBF, HIV exposure, and other maternal/child factors, with cognitive and emotional-behavioural development in children aged 7-11 years.

**Methods and findings**

The Vertical Transmission Study (VTS) supported EBF in HIV-positive and negative women; between 2012-2014 HIV-negative VTS children (332 HIV-exposed, 574 HIV-unexposed) were assessed on cognition (KABC-II), executive function (NEPSY-II), and emotional-behavioural functioning (CBCL). We developed population means by combining the VTS sample with 629 same-aged HIV-negative children from the local Demographic Platform. For each outcome we split the VTS sample into scores above or at/below each population mean and modelled each outcome using logistic regression analyses, overall and stratified by child sex. There was no demonstrated effect of EBF on overall cognitive functioning. EBF was associated with fewer conduct disorders overall (aOR0.44 [95%CI 0.3-0.7] p<=0.01) and there was weak evidence of better cognition for boys who had EBF for 2-5 months vs ≤1 month (Learning sub-scale aOR2.07 [95%CI 1.0-4.3] p=0.05). Other factors associated with better child cognition were higher maternal cognitive ability (aOR1.43 [95%CI 1.1-1.9] p=0.02 Sequential, aOR1.74 [95%CI 1.3-2.4] p<0.001 Planning sub-scales) and crèche attendance (aOR1.96 [95%CI 1.1-3.5] p=0.02 Sequential sub-scale). Factors positively associated with executive function were home stimulation (aOR1.36 [95%CI 1.0-1.8] p=0.04 Auditory Attention, 1.35 [95%CI 1.0-1.8] p=0.05 Response Set) and crèche (aOR1.74 [95%CI 1.0-3.0] p=0.05 Animal Sorting). Maternal mental health problems and parenting stress were associated with increased emotional-behavioural problems on the total Child Behaviour Checklist (CBCL) (aOR2.44 [95%CI 1.3-4.6] p=0.01; aOR7.04 [95%CI 4.2-11.9] p<0.001 respectively). Maternal HIV status was not associated with any outcomes in the overall cohort. Limitations include the non-randomised study design and lack of maternal mental health assessment at the child’s birth.

**Conclusions**

EBF was associated with fewer than average conduct disorders, and weakly with improved cognitive development in boys. Efforts to improve stimulation at home, reduce maternal stress, and enable crèche attendance are likely to improve executive function and emotional-behavioural development of children.

**Keywords**: Africa, child development, HIV, breastfeeding, exclusive breastfeeding

**Introduction**

There is strong evidence that exclusive breastfeeding (EBF) for six months, as recommended by the World Health Organization (WHO)(1), optimises infant nutrition, and substantially decreases mortality and morbidity from infectious diseases (2, 3). The relationship between EBF and cognitive development is less clear (4) (5), although studies in high income settings (6) (7) (8), a randomised trial from Belarus (9), and a recent study from Brazil (10) have shown positive associations. A large systematic review showed conflicting results depending on study design and rigour, and the number of factors adjusted for (4). The few studies from resource-limited settings were almost twice as likely to find no association. This suggests that confounding variables, including socio-economic status and maternal cognitive ability, affect the choice to breastfeed and the positive effects found. Measuring the duration of EBF accurately is challenging because of factors related to definition, timing, and duration of recall (11, 12), and many of the studies were limited by poor documentation of breastfeeding patterns (13, 14). Further limitations included small sample sizes (15, 16) and predominantly Caucasian populations, with only one small study from Africa (16) that found no association with cognitive development but some advantages for child behaviour in breastfed infants. There was no evidence from HIV prevalent areas where the long term effect of EBF on child development remains unquantified.

Studies exploring the link between EBF and later development have focused on core cognitive development, sometimes termed intelligence quotient (IQ). However, higher order cognitive function, termed executive function, is critical for later development, particularly the ability to function in society (17). Executive function coordinates and controls information processing, which is important for a child’s ability to manage emotions and behaviour, to follow rules, to concentrate and to form friendships. Thus executive function influences educational and social success (18). Executive function is susceptible to environmental influences and therefore an important intervention target (19). In addition, few breastfeeding studies have examined emotional-behavioural development, an important outcome affected by early life factors, which predicts later educational achievement.

The Vertical Transmission Study (VTS) (2001-2006) supported HIV-positive and negative women to EBF in a rural area of South Africa before antiretroviral treatment became available (20), providing the first evidence that EBF reduced the risk of postnatal HIV transmission (21), and was associated with significant benefits for children’s health and growth up to two years of age (22, 23) (Registration NCT01948557 National Institute of Health ClinicalTrials.gov). Here we investigate the association between EBF, HIV exposure and other early and current life factors, and later cognitive development, executive function and emotional-behavioural development in VTS children now aged 7 to 11 years. We accounted for maternal cognitive function, home stimulation, pre-school attendance, maternal/caregiver stress and mental health, and hypothesized that EBF would result in improved longer term development in children, despite exposure to HIV and poverty.

**Methods**

Ethics permission for this study was granted by the Biomedical Research Ethics Committee (BREC), University of KwaZulu-Natal, South Africa (BF184/12). Women were contacted by telephone or a home visit to ask if they would be interested in this study. Those who agreed were then visited by a field worker who explained, and provided written details of, the study and obtained written informed consent from the mother and primary caregiver (if this was not the child’s mother).

The VTS, a non-randomised, prospective, intervention cohort study, was implemented between 2001 and 2006 from the Africa Centre for Population Health which also hosts a Demographic and Health Surveillance (DSS) platform (24). This lay-counsellor, home-based intervention, was designed to support mothers to EBF for the first 180 days of life (25). Between 2012 and 2014 we re-enrolled HIV-negative children (aged 7-11 years) born to HIV-positive (‘exposed’) and HIV-negative (‘unexposed’) mothers from the VTS cohort; HIV-infected children were not re-enrolled because they have different developmental trajectories (26).

To establish a comparative population mean for the developmental outcomes, (in the absence of appropriate normative data for validated cognitive assessments) we assessed 630 (485 unexposed; 145 exposed) same-aged HIV-negative children from the DSS, not included in the VTS, and combined these with the VTS sample. Mothers in the DSS group were exposed to the same antenatal care at local clinics, including messages regarding HIV and infant feeding, but not the home-based intervention to support EBF. We aimed to re-recruit all available 1289 VTS children meeting the inclusion criteria, of whom 935 (75%) were enrolled and 906 (70%) fully assessed. To establish a robust population mean we used the population platform of the Africa Centre for Population Health surveillance to identify all 1226 resident children, matched for age and HIV exposure to the VTS children, but who had not been exposed to the VTS intervention. Of these, 844 children met eligibility criteria and 657 (77%) enrolled and 630 (75%) completed assessments.

This analysis includes the developmental outcomes of the VTS children, for all of whom we have accurate data on infant feeding and HIV exposure; their outcomes are related to the population means. Children were enrolled if both mother and child were alive, child was resident in the research area, mother and child’s current HIV status was known, and, for the DSS children, if the HIV status during pregnancy was known, mother received antenatal services in the study community, and the maternal-held child Road-to-Health Card was available.

**Outcome measures**

*Child Cognition:* To assess the cognitive development we used the full Kaufman Assessment Battery for Children (KABC-II) (27). This has four sub-scales, each with sub-tests, which measure: audio and visual memory and memory span (‘Sequential processing’); spatial and visual perception, reasoning and maths ability (‘Simultaneous processing’); focused and selective attention, and ability to store auditory and visual stimuli simultaneously (‘Learning ability’); and decision making ability (‘Planning’). There is an additional subtest to assess reasoning and language development ‘Riddles’). After discussion with experts including the authors of the KABC-II, to be more culturally appropriate we substituted a sub-test in the Learning Ability sub-scale (‘Atlantis’/ ‘Atlantis delayed’ replaced ‘Rebus’/ ‘Rebus delayed’). The KABC-II has been used in low-middle income countries, and validated in Africa (28) (Cronbach’s α=0.75).

*Child Executive function:* Three sub-tests from the executive function domain of the Neuropsychological Assessment (NEPSY-II) (29) were used: Animal Sorting (inhibition, planning, cognitive flexibility), Auditory Attention (vigilance, selective/ sustained auditory attention) and Response Set (inhibition of previously learned stimuli).

All subtest raw scores for both NEPSY-II and KABC-II were transformed to scaled scores, according to the child’s age, using standardised tables published by the test developers.

*Child emotional and behavioural functioning*: We used the parent-reported Child Behaviour Checklist (CBCL) (30), which has been validated across multiple cultural settings (31). This includes 120-items in two subscales: ‘Internalising disorders’ and ‘Externalising disorders’, and a composite Total score. A high score indicates more problems. Scores were normed using multicultural Rating-to-Score norming software to produce normed t-tests for the Total score, the two subscales, and the six Diagnostic and Statistical Manual (DSM) disorders: Affective, Anxious, Somatic, Attention Deficit Hyperactivity Disorder, Oppositional and Conduct disorders (Cronbach’s α=0.94).

**Maternal mental health measures**

All psychometric measures had been used in the population previously; clinical algorithms for depression and anxiety were used.

* *Depression and Anxiety*: measured using the Patient Health Questionnaire Depression (PHQ-9) and General Anxiety (GAD-7) Scales (32, 33), identifying depressive or anxiety symptoms with symptom frequency and severity.
* *Alcohol:* the WHO Alcohol Use Disorders Identification Test (AUDIT-6), assessed alcohol use and severity (34).
* *Parenting Stress:* measured using the Parenting Stress Index Short Form (PSI-36), a 36-item scale measuring stress related to the parental role, the parent-child relationship and the degree to which the parent finds the child difficult (35).

The home environment was assessed using a locally adapted version of the HOME inventory (36). Maternal cognitive ability was assessed using the Standard Raven’s Progressive Matrix (37).

**Data collection**

Data were collected over three visits between September 2012 and September 2014. Study consent was obtained at Visit 1; current socio-economic and health data, mothers’ mental health and cognitive ability at Visit 2; and children’s cognition and executive function at Visit 3. When the mother was not the primary caregiver, mental health assessments were completed by the child’s primary caregiver. Assessments were conducted by graduate-level research assistants with 3-5 years’ child developmental assessment experience. The median number of days between Visit 2 and 3 was 18 days.

**Statistical analyses**

Analyses were based on data extracted on 30-Oct-2014 and conducted using STATA version 13. For each outcome we calculated a population mean from all VTS and DSS children, then created a binary indicator by splitting the VTS group into those scoring above or at/below the mean. For the HOME assessment and Raven’s score we created a low/high indicator consisting of equal-size groups by splitting the VTS sample based on their median. In the VTS, daily feeding data were collected at weekly intervals. We defined EBF as the total number of days in the first six months that the child received only breastmilk and then divided this number by 30, into months, irrespective of whether the days were sequential. We previously reported (25) that approximately 40% of VTS women interrupted EBF at some point in the first six months, mostly by giving water or formula milk, of whom approximately 60% returned to EBF within two days. We considered that the total number of days of EBF in the first six months were more likely to have an impact on child development than whether they were sequential or not, and we did not wish to exclude children who had received breastmilk for nearly all 180 days except for one or two days when they received breastmilk and other fluids. We identified relevant factors based on the existing literature, and theoretical and conceptual reasoning, including child, maternal, early life, socioeconomic, and household factors related to child development; we did not apply any stepwise regression techniques. For selection of the most relevant socioeconomic variable, we used principal components analysis to identify the top variables that explained the overall variance. We modelled each of the outcomes using complete case logistic regression analyses, accounting for intra-mother correlation (for twins). We included child sex, age, birth order, maternal age; early life factors included birth-weight, maternal HIV-status during pregnancy, months of EBF, urban/rural residence, ownership of fridge (wealth indicator), maternal education and whether the mother was the main income provider at the time of the child’s birth; and other factors including maternal current HIV-status, cognitive ability, mental health and parenting stress, crèche exposure, current indicators of perception of household wealth and HOME assessment score. Sex differences in cognitive development exist at primary school age(38), and we also estimated sex-stratified logistic regression models, using the same outcomes.

We explored several approaches to modelling the developmental data, including continuous outcomes (see S1 Table), and upper versus lower quintiles, as well as other methods of categorising the EBF data, including cumulative, sequential, days of EBF and ever/never EBF, but the results were not substantially different.

**Results**

The sample

By end of VTS follow-up in September 2006, when children were aged two years, 1289 HIV-negative children were alive, of whom 941 were eligible for re-enrolment and 906 were assessed (Figure 1). Compared to HIV-unexposed, exposed children were more likely to have a mother who was older and the main income provider, less likely to have been EBF to six months and to have attended crèche, and more likely to have a primary caregiver with a current mental health disorder (Table 1). Compared to children included in the current analysis, the 383 VTS children excluded were more likely to have a younger HIV-uninfected mother with more years of education at the time of pregnancy and were less likely to be low birth-weight (Table 1).

**Figure 1**: Consort diagram of VTS HIV-uninfected children included in the current follow up

**Table 1**: Characteristics of children and mothers included and excluded from the analyses of the Vertical Transmission Study (VTS) cohort

|  |  |  |
| --- | --- | --- |
|  | **Total VTS included (n=906) by HIV exposure** | **Total VTS (n=1289) included and excluded** |
| **Variable** | ***Unexposed*****n=574 (63%)** | ***Exposed*** **n=332 (37%)** | **p-value** | ***Included*****n=906 (70%)** | ***Excluded f*****n=383 (30%)** | **p-value** |
| ***Child Sex***  |  |  |  |  |  |  |
| Female | 288 (50.2) | 169 (50.9) | 0.832 | 457 (50.4) | 198 (51.7) | 0.680 |
| Male | 286 (49.8) | 163 (49.1) |  | 449 (49.6) | 185 (48.3) |  |
| ***Child Age (Current)*** |  |  |  |  |  |  |
| 8 years | 23 (4.0) | 20 (6.0) | **< 0.001** | 43 (4.8) |  |  |
| 9 years | 289 (50.3) | 114 (34.4) |  | 403 (44.5) |  |  |
| 10 years | 238 (41.5) | 140 (42.3) |  | 378 (41.8) |  |  |
| 11 years | 24 (4.2) | 57 (17.2) |  | 81 (9.0) |  |  |
| Missing | 0 | 1 |  | 1 |  |  |
| ***Mother's age (at birtha)***  |  |  |  |  |  |  |
| Less than 20 years | 154 (26.8) | 34 (10.2) | **< 0.001** | 187 (20.6) | 101 (26.4) | **< 0.001** |
| 20-29 years | 249 (43.4) | 190 (57.2) |  | 4442 (48.8) | 215 (56.1) |  |
| 30+ years | 171 (29.8) | 108 (32.5) |  | 277 (30.6) | 67 (17.5) |  |
| ***Mother's education (at birth)***  |  |  |  |  |  |  |
| None | 47 (8.2) | 21 (6.3) | 0.535 | 68 (7.5) | 23 (6.0) | **0.002** |
| Primary | 216 (37.6) | 137 (41.3) |  | 353 (39.0) | 113 (29.5) |  |
| Some secondary | 207 (36.1) | 111 (33.4) |  | 318 (35.1) | 149 (38.9) |  |
| Completed secondary and post | 104 (18.1) | 63 (19.0) |  | 167 (18.4) | 98 (25.6) |  |
| ***Birth-weight*** |  |  |  |  |  |  |
| Low birth-weightb | 47 (8.5) | 42 (13.7) | **0.018** | 89 (10.4) | 22 (6.1) | **0.017** |
| Normal birth-weight | 503 (91.5) | 265 (86.3) |  | 768 (89.6) | 340 (93.9) |  |
| Missing | 24 | 25 |  | 49 | 21 |  |
| ***Exclusive breastfeedingc*** |  |  |  |  |  |  |
| 0-1 months | 44 (7.7) | 67 (20.2) | **< 0.001** | 111 (12.3) | 49 (12.8) | 0.460 |
| 2-5 months | 167 (29.1) | 101 (30.5) |  | 268 (29.6) | 125 (32.7) |  |
| 6 months | 363 (63.2) | 163 (49.2) |  | 526 (58.1) | 208 (54.5) |  |
| Missing | 0 | 1 |  | 1 | 1 |  |
| ***Birth order***  |  |  |  |  |  |  |
| Birth order 1-2 | 346 (60.3) | 176 (53.2) | **0.015** | 522 (57.7) |  |  |
| Birth order 3-4 | 115 (20.0) | 94 (28.4) |  | 209 (23.1) |  |  |
| Birth order 5+ | 113 (19.7) | 61 (18.4) |  | 174 (19.2) |  |  |
| Missing | 0 | 1 |  | 1 |  |  |
| ***Mother's HIV status*** |  |  |  |  |  |  |
| Negative | 403 (70.5) | 0 (0.0) | **< 0.001** | 403 (44.6) | 207 (54.0) | **0.002** |
| Positive pregnancy | 0 (0.0) | 332 (100.0) |  | 332 (36.7) | 176 (46.0) |  |
| Positive since pregnancy | 169 (29.5) | 0 (0.0) |  | 169 (18.7) |  |  |
| Missing | 2 | 0 |  | 6 | 0 |  |
| ***Residence (at bBirth)*** |  |  |  |  |  |  |
| Rural  | 377 (65.7) | 177 (53.3) | **< 0.001** | 554 (61.1) | 241 (62.9) | 0.549 |
| Urban  | 197 (34.3) | 155 (46.7) |  | 352 (38.9) | 142 (37.1) |  |
| ***Main income (at birth)*** |  |  |  |  |  |  |
| Other | 539 (94.1) | 286 (86.4) | **< 0.001** | 825 (91.3) | 355 (92.9) | 0.319 |
| Mother | 34 (5.9) | 45 (13.6) |  | 79 (8.7) | 27 (7.1) |  |
| Missing | 1 | 1 |  | 2 | 1 |  |
| ***Owns fridge (at aBirth)*** |  |  |  |  |  |  |
| Fridge No | 328 (57.2) | 204 (61.6) | 0.196 | 532 (58.8) | 220 (57.6) | 0.676 |
| Fridge Yes | 245 (42.8) | 127 (38.4) |  | 372 (41.2) | 162 (42.4) |  |
| Missing | 1 | 1 |  | 2 | 1 |  |
| ***Perception wealth (Current)*** |  |  |  |  |  |  |
| Very comfortable | 56 (9.8) | 30 (9.1) | 0.860 | 86 (9.5) |  |  |
| Getting by | 340 (59.2) | 202 (61.0) |  | 542 (59.9) |  |  |
| Extremely poor | 178 (31.0) | 99 (29.9) |  | 277 (30.6) |  |  |
| Missing | 0 | 1 |  | 1 |  |  |
| ***Creched*** |  |  |  |  |  |  |
| No creche | 37 (6.4) | 35 (10.5) | **0.028** | 72 (7.9) |  |  |
| Attended creche | 537 (93.6) | 297 (89.5) |  | 834 (92.1) |  |  |
| ***Maternal mental healthe(Current)*** |  |  |  |  |  |  |
| No mental disorders | 525 (91.5) | 289 (87.3) | **0.045** | 814 (89.9) |  |  |
| Depression or anxiety or alcohol use | 49 (8.5) | 42 (12.7) |  | 91 (10.1) |  |  |
| Missing | 0 | 1 |  | 1 |  |  |
| ***Parenting stress (Current)*** |  |  |  |  |  |  |
| Parenting stress ≤ 90 | 493 (85.9) | 280 (84.3) | 0.525 | 773 (85.3) |  |  |
| Parenting stress ≥ 90 | 81 (14.1) | 52 (15.7) |  | 133 (14.7) |  |  |

Footnotes (apply to Tables 1-9)

*Bold numbers indicate a p value <0.05*

*a ‘Birth indicates that the variable relates to when the child was born as opposed to the time of follow-up at 7-10 years; Current indicates that the variable relates to the time of follow-up in this study when the child was aged between 7-10 years*

*b Low birth-weight was defined as <2.5 kg*

*c Exclusive breastfeeding (EBF) for this analysis was defined as the number of days when the child only received breastmilk and no other fluids or solids; the total number of days was divided by 30 to categorise the number of months of EBF*

*d Creche is a non-compulsory, non-governmental, pre-school; children start primary school in South Africa aged 7 years*

*eProvisional depression diagnosis determined byPHQ9 diagnostic algorithm required at least one Criteria A (mood; loss of interest) and 2-4 Criteria B (weight; sleep; agitation/retardation ; fatigue; guilt; concentration; suicidality) for more than  half the days. Provisional anxiety diagnosis required meeting Criteria A (anxiety) and ≥3 Criteria B (worry; restlessness; fatigue; concentration; irritability; sleep) for more than half the days.*

*fChild age and birth order are not shown for the excluded children, some of whom died or were lost to follow-up. Other variables omitted for the excluded children are factors measured since the VTS cohort, including current perception of wealth, attendance at crèche, caregiver mental health and parenting stress.*

Cognitive outcomes

None of the cognitive development measurements were significantly associated with EBF or maternal HIV status in adjusted analyses (Table 2). In multivariable analyses, the only variable significantly positively associated with performance on all cognitive sub-scales was maternal cognitive ability (measured using the Standard Raven’s Progressive Matrix) (Table 2). Boys were approximately 30% less likely than girls to score above the mean in the Sequential Processing sub-scale which tests audio and visual memory, and memory span (aOR 0.71 [95% CI 0.5-0.9], p=0.03), whilst children who had attended crèche were almost twice as likely to score above the mean (aOR 1.96 [95% CI 1.1-3.5], p= 0.02). Children older at assessment performed worse on Riddles (aOR 0.40 [95% CI 0.2-1.0], p=0.05).

Table 2 Factors associated with children's cognitive outcomes measured by the Kauffman Assessment Battery (KABC-II)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Sequential (N=825)** | **Planning (N=825)** | **Learning (N=825)** | **Simultaneous (N=825)** | **Riddles (N=824)** |
|  | **OR [CI]** | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]** |
| ***Child Sex*** |  |  |  |  |  |  |  |  |  |  |
| Female | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Male | **0.69\*\* [0.5-0.9]**  | **0.71\* [0.5-0.9]**  | **0.74\* [0.6-1.0]**  | 0.77 [0.6-1.0]  | 1.13 [0.9-1.5]  | 1.18 [0.9-1.6]  | 1.22 [0.9-1.7]  | 1.26 [0.9-1.7]  | 0.92 [0.7-1.2]  | 0.91 [0.7-1.2]  |
| ***Child Age (Current)*** |  |  |  |  |  |  |  |  |  |  |
| 8 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 9 years | 1.06 [0.5-2.1]  | 1.16 [0.6-2.3]  | 1.12 [0.6-2.0]  | 1.29 [0.7-2.4]  | 1.20 [0.6-2.3]  | 1.17 [0.6-2.3]  | 0.66 [0.4-1.2] | 0.68 [0.4-1.3]  | 0.84 [0.4-1.6]  | 0.99 [0.5-2.0]  |
| 10 years | 0.81 [0.4-1.6]  | 0.93 [0.5-1.9]  | 0.96 [0.5-1.8]  | 1.21 [0.6-2.3]  | 1.06 [0.6-2.0]  | 1.02 [0.5-2.0]  | **0.47\* [0.3-0.9]**  | **0.49\* [0.3-1.0]**  | 0.59 [0.3-1.1]  | 0.70 [0.3-1.4]  |
| 11 years | 0.75 [0.3-1.7]  | 0.91 [0.4-2.1]  | 0.60 [0.3-1.3]  | 0.85 [0.4-1.9]  | 1.12 [0.5-2.4]  | 1.17 [0.5-2.6]  | 0.53 [0.2-1.1]  | 0.57 [0.3-1.3]  | **0.34\* [0.1-0.8]**  | **0.40\* [0.2-1.0]**  |
| ***Mother's Age ( at birth)*** |  |  |  |  |  |  |  |  |  |  |
| Less than 20 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 20-29 years | 1.03 [0.7-1.5]  | 1.01 [0.7-1.5]  | 0.88 [0.6-1.3]  | 0.81 [0.5-1.2]  | 1.14 [0.8-1.7]  | 1.16 [0.8-1.8]  | 1.26 [0.9-1.8]  | 1.11 [0.7-1.7]  | 1.24 [0.8-1.8]  | 1.08 [0.7-1.7]  |
| 30+ years | 1.11 [0.7-1.7]  | 1.52 [0.8-2.7]  | 0.82 [0.6-1.2]  | 0.80 [0.4-1.4]  | 1.21 [0.8-1.8]  | 1.90 [1.0-3.4]  | 1.37 [0.9-2.0]  | 1.16 [0.6-2.1]  | 1.12 [0.7-1.7]  | 1.09 [0.6-2.0]  |
| ***Maternal IQ (Current)a*** |  |  |  |  |  |  |  |  |  |  |
| Low Raven’s | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Raven’s | **1.60\*\* [1.2-2.1]**  | **1.43\* [1.1-1.9]**  | **2.04\*\*\* [1.5-2.7]**  | **1.74\*\*\* [1.3-2.4]**  | **1.84\*\*\* [1.4-2.4]**  | **1.64\*\* [1.2-2.2]**  | **1.60\*\* [1.2-2.1]**  | **1.46\* [1.0-2.0]**  | **1.81\*\*\* [1.4-2.4]**  | **1.60\*\* [1.2-2.2]**  |
| ***Mother's Education ( at birth)*** |  |  |  |  |  |  |  |  |  |  |
| None | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Primary | 0.96 [0.5-1.7]  | 0.97 [0.5-1.8]  | 1.00 [0.6-1.8]  | 1.05 [0.6-1.9]  | 1.11 [0.6-2.0]  | 0.97 [0.5-1.8]  | 1.31 [0.7-2.3]  | 1.31 [0.7-2.4]  | 0.93 [0.5-1.7]  | 0.92 [0.5-1.8]  |
| Some secondary | 1.23 [0.7-2.2]  | 1.13 [0.6-2.2]  | 1.50 [0.8-2.7]  | 1.42 [0.8-2.7]  | 1.34 [0.7-2.4]  | 1.12 [0.6-2.1]  | 1.36 [0.8-2.4]  | 1.42 [0.7-2.7]  | 1.38 [0.7-2.6]  | 1.30 [0.7-2.6]  |
| Completed secondary/post | 1.70 [0.9-3.1]  | 1.40 [0.7-2.8]  | **2.01\* [1.0-3.7]**  | 1.66 [0.8-3.4]  | **2.21\* [1.2-4.1]**  | 1.52 [0.8-3.0]  | **2.46\*\* [1.3-4.6]**  | **2.15\* [1.0-4.4]**  | **1.99\* [1.0-3.8]**  | 1.59 [0.8-3.3]  |
| ***Birthweight*** |  |  |  |  |  |  |  |  |  |  |
| Low Birthweight | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Normal Birthweight | 1.36 [0.9-2.2]  | 1.34 [0.8-2.2]  | 1.39 [0.9-2.2]  | 1.42 [0.9-2.3]  | 1.42 [0.9-2.2]  | 1.35 [0.8-2.2]  | 1.48 [0.9-2.3]  | 1.48 [0.9-2.4]  | 1.61 [1.0-2.7]  | 1.58 [0.9-2.8]  |
| ***Exclusive Breastfeeding*** |  |  |  |  |  |  |  |  |  |  |
| 0-1 months | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2-5 months | 1.09 [0.7-1.7]  | 1.27 [0.8-2.1]  | 0.93 [0.6-1.5]  | 0.96 [0.6-1.6]  | 0.93 [0.6-1.5]  | 1.16 [0.7-1.9]  | 1.02 [0.6-1.6]  | 1.34 [0.8-2.2]  | 0.76 [0.5-1.2]  | 1.07 [0.6-1.8]  |
| 6 months | 1.01 [0.7-1.6]  | 1.23 [0.8-2.0]  | 0.75 [0.5-1.1]  | 0.80 [0.5-1.3]  | 1.04 [0.7-1.6]  | 1.29 [0.8-2.1]  | 0.94 [0.6-1.4] | 1.29 [0.8-2.1]  | 0.77 [0.5-1.2]  | 1.18 [0.7-1.9]  |
| ***Birth order (Birth)*** |  |  |  |  |  |  |  |  |  |  |
| Birth order 1-2 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Birth order 3-4 | 0.92 [0.7-1.3]  | 0.87 [0.6-1.3]  | 0.86 [0.6-1.2]  | 1.15 [0.8-1.7]  | 0.91 [0.7-1.3]  | 0.84 [0.6-1.3]  | 1.06 [0.8-1.5]  | 1.08 [0.7-1.6]  | 1.15 [0.8-1.6]  | 1.27 [0.8-2.0]  |
| Birth order 5+ | 0.84 [0.6-1.2]  | 0.72 [0.4-1.3]  | 0.87 [0.6-1.2]  | 1.33 [0.8-2.3]  | 0.76 [0.5-1.1]  | 0.61 [0.3-1.0]  | 1.17 [0.8-1.7]  | 1.25 [0.7-2.2]  | 0.81 [0.6-1.2]  | 1.07 [0.6-2.0]  |
| ***Mother's HIV status*** |  |  |  |  |  |  |  |  |  |  |
| Negative | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Positive pregnancy | 1.03 [0.8-1.4]  | 1.13 [0.8-1.6]  | 0.75 [0.5-1.0]  | 0.83 [0.6-1.2]  | 1.11 [0.8-1.5]  | 1.23 [0.9-1.7]  | 0.92 [0.7-1.2]  | 0.99 [0.7-1.4]  | 1.10 [0.8-1.5]  | 1.29 [0.9-1.9]  |
| Positive since pregnancy | 0.81 [0.6-1.2]  | 0.83 [0.5-1.2]  | **0.66\* [0.5-1.0]**  | 0.69 [0.5-1.0]  | 1.04 [0.7-1.5]  | 1.18 [0.8-1.7]  | **0.60\* [0.4-0.9]**  | 0.69 [0.5-1.0]  | 0.84 [0.6-1.3]  | 0.96 [0.6-1.5]  |
| ***Residence (at birth)*** |  |  |  |  |  |  |  |  |  |  |
| Rural  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Urban  | **1.39\* [1.0-1.8]**  | 1.27 [0.9-1.7]  | **1.38\* [1.0-1.8]**  | 1.27 [0.9-1.7]  | 1.24 [0.9-1.6]  | 1.11 [0.8-1.5]  | **1.48\*\* [1.1-2.0]**  | 1.22 [0.9-1.7]  | **1.54\*\* [1.1-2.1]**  | 1.27 [0.9-1.7]  |
| ***Income provider (at birth)*** |  |  |  |  |  |  |  |  |  |  |
| Other | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Mother | 0.93 [0.6-1.5]  | 0.83 [0.5-1.4]  | 0.75 [0.5-1.2]  | 0.69 [0.4-1.2]  | 0.95 [0.6-1.5]  | 0.88 [0.5-1.5]  | 1.44 [0.9-2.3]  | 1.21 [0.7-2.1]  | 1.14 [0.7-1.9]  | 1.05 [0.6-1.9]  |
| ***Owns fridge (at birth)*** |  |  |  |  |  |  |  |  |  |  |
| Fridge No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Fridge Yes | 1.19 [0.9-1.6]  | 1.01 [0.7-1.4]  | **1.38\* [1.0-1.8]**  | 1.14 [0.8-1.5]  | 1.28 [1.0-1.7]  | 1.16 [0.9-1.6]  | 1.28 [1.0-1.7]  | 1.10 [0.8-1.5]  | **1.45\* [1.1-1.9]**  | 1.18 [0.9-1.6]  |
| ***Perception wealth(Current)*** |  |  |  |  |  |  |  |  |  |  |
| Very comfortable | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Getting by | 0.63 [0.4-1.0]  | 0.70 [0.4-1.2]  | 0.85 [0.5-1.4]  | 0.91 [0.5-1.5]  | 0.98 [0.6-1.6]  | 1.08 [0.7-1.8]  | 1.05 [0.7-1.7]  | 1.13 [0.7-1.9]  | 0.81 [0.5-1.3]  | 0.81 [0.5-1.3]  |
| Extremely poor | 0.65 [0.4-1.1]  | 0.77 [0.4-1.3]  | 0.80 [0.5-1.3]  | 1.02 [0.6-1.8]  | 0.79 [0.5-1.3]  | 0.97 [0.6-1.7]  | 0.90 [0.5-1.5]  | 1.13 [0.7-1.9]  | 0.61 [0.4-1.0]  | 0.72 [0.4-1.3]  |
| ***Creche*** |  |  |  |  |  |  |  |  |  |  |
| No creche | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Attended creche | **2.38\*\* [1.4-4.2]**  | **1.96\* [1.1-3.5]**  | 1.57 [0.9-2.7] | 1.14 [0.6-2.0]  | 1.17 [0.7-2.0]  | 0.99 [0.6-1.8]  | 1.21 [0.7-2.1]  | 1.00 [0.6-1.7]  | 1.22 [0.7-2.2]  | 0.87 [0.4-1.6]  |
| ***MC-Home b(Current)*** |  |  |  |  |  |  |  |  |  |  |
| Low Total | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Total | 1.06 [0.8-1.4]  | 0.93 [0.7-1.2]  | 1.22 [0.9-1.6]  | 1.12 [0.8-1.5]  | 1.29 [1.0-1.7]  | 1.19 [0.9-1.6]  | 1.11 [0.8-1.5]  | 1.07 [0.8-1.4]  | 1.02 [0.8-1.4]  | 0.94 [0.7-1.3]  |
| ***Maternal mental health (Current)*** |  |  |  |  |  |  |  |  |  |  |
| No mental disorders | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Depression or anxiety or alcohol use | 1.45 [0.9-2.3]  | 1.53 [0.9-2.6]  | 0.88 [0.5-1.4]  | 1.01 [0.6-1.7]  | 0.64 [0.4-1.1]  | 0.68 [0.4-1.2]  | 0.72 [0.4-1.2]  | 0.78 [0.5-1.3]  | 0.81 [0.5-1.4]  | 0.74 [0.4-1.3]  |
| ***Parenting stress(Current)*** |  |  |  |  |  |  |  |  |  |  |
| Parenting stress ≤ 90 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Parenting stress ≥ 90 | 0.91 [0.6-1.3]  | 0.97 [0.6-1.5]  | **0.66\* [0.4-1.0]**  | 0.74 [0.5-1.1]  | 0.74 [0.4-1.1]  | 0.82 [0.5-1.3]  | 0.75 [0.5-1.1]  | 0.83 [0.5-1.3]  | 0.99 [0.7-1.5]  | 1.14 [0.7-1.8]  |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the confidence intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*ORs based on bivariate logistic regression of the outcome on the covariate. AORs based on multivariate logistic regression on the outcomes including all covariates*

*Sequential Processing: measures audio and visual memory and memory span*

*Simultaneous Processing: measures spatial and visual perception, reasoning and maths ability*

*Learning ability: measures focused and selective attention, and ability to store auditory and visual stimuli simultaneously*

*Planning: measures decision making ability*

*Riddles: measures reasoning and language development*

Executive Function

None of the executive function measures were significantly associated with EBF duration, maternal HIV or child sex (Table 3). Compared to children whose mothers were aged less than 20 years, those with mothers aged 20-29 years at their birth were almost twice as likely to score above the mean on the Animal Sorting sub-test (aOR 1.82 [95% CI 1.2-2.8], p=0.01), as were children whose mother was the main income provider during their infancy (aOR 1.81 [95% CI 1.0-3.1], p=0.03) and those who had attended crèche (aOR 1.74 [95% CI 1.0-3.0], p=0.05). For the Auditory Attention sub-test, compared to children aged eight years, those aged nine and 10 years were over three (aOR 3.38 [95% CI 1.6-7.3], p=0.01) and four times (aOR 4.56 [95% CI 2.1-9.9], p<0.001) respectively more likely to perform above average. Children with better stimulation at home (i.e. a HOME score above the median) were more likely to perform above the mean in Auditory Attention (aOR 1.36 [95% CI 1.0-1.8], p=0.04) and Response Set sub-tests (aOR 1.35 [95% CI 1.0-1.8], p=0.05).

Table 3 Factors associated with children's executive function measured by Developmental Neuropsychological Assessment (NEPSY)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Animal sorting (N=824)** | **Auditory attention (N=821)** | **Response set (N=820)** |
|  | **OR [CI]**  | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]**  |
| ***Sex*** |  |  |  |  |  |  |
| Female | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Male | 0.93 [0.7-1.2]  | 0.93 [0.7-1.2]  | 0.83 [0.6-1.1]  | 0.83 [0.6-1.1]  | 0.92 [0.7-1.2]  | 0.97 [0.7-1.3]  |
| ***Child Age (Current)*** |  |  |  |  |  |  |
| 8 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 9 years | 0.63 [0.3-1.3]  | 0.70 [0.3-1.5]  | **3.26\*\*[1.5-7.0]**  | **3.38\*\* [1.6-7.3]**  | 1.77 [0.9-3.5]  | 1.60 [0.8-3.2]  |
| 10 years | 0.55 [0.3-1.1]  | 0.65 [0.3-1.4]  | **4.35 \*\*\*[2.0-9.3]**  | **4.56\*\*\* [2.1-9.9]**  | 1.55 [0.8-3.1]  | 1.39 [0.7-2.8]  |
| 11 years | 0.72 [0.3-1.6]  | 0.87 [0.4-2.1]  | 1.83 [0.8-4.4]  | 1.98 [0.8-4.8]  | 0.79 [0.4-1.7]  | 0.73 [0.3-1.7]  |
| ***Mother's Age (at birth)*** |  |  |  |  |  |  |
| Less than 20 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 20-29 years | **1.98\*\*\* [1.4-2.9]**  | **1.82\*\* [1.2-2.8]**  | 1.18 [0.8-1.7]  | 1.08 [0.7-1.7]  | 0.71 [0.5-1.1]  | 0.72 [0.5-1.1]  |
| 30+ years | **1.56\* [1.1-2.3]**  | 1.60 [0.9-2.9]  | **1.53\* [1.0-2.3]**  | 1.53 [0.8-2.8]  | **0.59\* [0.4-0.9]**  | 0.69 [0.4-1.3]  |
| ***Maternal IQ (Current)a*** |  |  |  |  |  |  |
| Low Raven’s | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Raven’s | 1.08 [0.8-1.4]  | 0.96 [0.7-1.3]  | 1.17 [0.9-1.5]  | 1.10 [0.8-1.5]  | 1.23 [0.9-1.6]  | 1.05 [0.8-1.4]  |
| ***Mother's Education (at birth)*** |  |  |  |  |  |  |
| None | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Primary | 1.12 [0.6-2.0]  | 1.09 [0.6-2.0]  | 0.56 [0.3-1.0]  | 0.62 [0.3-1.2]  | 1.06 [0.6-1.9]  | 1.02 [0.6-1.9]  |
| Some secondary | 1.27 [0.7-2.3]  | 1.23 [0.6-2.3]  | 0.75 [0.4-1.3]  | 0.99 [0.5-1.9]  | 1.61 [0.9-2.9]  | 1.47 [0.8-2.8]  |
| Completed secondary/post | **1.87\* [1.0-3.5]**  | 1.50 [0.7-3.0]  | 0.80 [0.4-1.5]  | 0.96 [0.5-2.0]  | 1.41 [0.8-2.6]  | 1.33 [0.7-2.7]  |
| ***Birthweight*** |  |  |  |  |  |  |
| Low Birthweight | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Normal Birthweight | 1.40 [0.9-2.2]  | 1.48 [0.9-2.5]  | 0.99 [0.6-1.6]  | 0.91 [0.6-1.4]  | 1.12 [0.7-1.8]  | 1.12 [0.7-1.8]  |
| ***Exclusive Breastfeeding*** |  |  |  |  |  |  |
| 0-1 months | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2-5 months | 0.91 [0.6-1.5]  | 1.17 [0.7-1.9]  | 0.75 [0.5-1.2]  | 0.68 [0.4-1.1]  | 1.15 [0.7-1.9]  | 1.13 [0.7-1.9]  |
| 6 months | 0.98 [0.6-1.5]  | 1.35 [0.8-2.2]  | 0.78 [0.5-1.2]  | 0.69 [0.4-1.1]  | 1.08 [0.7-1.7]  | 1.09 [0.7-1.8]  |
| ***Birth order (Birth)*** |  |  |  |  |  |  |
| Birth order 1-2 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Birth order 3-4 | 1.13 [0.8-1.6]  | 0.92 [0.6-1.4]  | 1.15 [0.8-1.6]  | 1.14 [0.8-1.7]  | 0.78 [0.6-1.1]  | 0.98 [0.6-1.5]  |
| Birth order 5+ | 0.90 [0.6-1.3]  | 0.77 [0.4-1.4]  | 1.21 [0.8-1.7]  | 1.11 [0.6-2.0]  | **0.66\* [0.5-0.9]**  | 0.94 [0.5-1.7]  |
| ***Mother's HIV status*** |  |  |  |  |  |  |
| Negative | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Positive pregnancy | 1.12 [0.8-1.5]  | 1.02 [0.7-1.4]  | 0.91 [0.7-1.2]  | 0.96 [0.7-1.4]  | 0.87 [0.6-1.2]  | 1.06 [0.8-1.5]  |
| Positive since pregnancy | 0.77 [0.5-1.1]  | 0.85 [0.6-1.3]  | 0.86 [0.6-1.2]  | 0.90 [0.6-1.4]  | 1.08 [0.7-1.6]  | 1.03 [0.7-1.6]  |
| ***Residence (at birth)*** |  |  |  |  |  |  |
| Rural  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Urban  | **1.49\*\* [1.1-2.0]**  | 1.32 [1.0-1.8]  | 0.88 [0.7-1.2]  | 0.90 [0.7-1.2]  | 0.98 [0.7-1.3]  | 0.95 [0.7-1.3]  |
| ***Income provider (at birth)*** |  |  |  |  |  |  |
| Other | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Mother | **1.84\* [1.1-3.1]**  | **1.81\* [1.0-3.1]**  | 0.89 [0.5-1.5]  | 0.86 [0.5-1.5]  | 0.81 [0.5-1.3]  | 0.99 [0.6-1.7]  |
| ***Owns fridge (at birth)*** |  |  |  |  |  |  |
| Fridge No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Fridge Yes | 1.29 [1.0-1.7]  | 1.19 [0.9-1.6]  | 1.21 [0.9-1.6]  | 1.19 [0.9-1.6]  | 1.02 [0.8-1.4]  | 1.05 [0.8-1.4]  |
| ***Perception wealth(Current)*** |  |  |  |  |  |  |
| Very comfortable | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Getting by | 0.97 [0.6-1.6]  | 1.14 [0.7-1.9]  | 1.17 [0.7-1.9]  | 1.20 [0.7-2.0]  | 1.05 [0.6-1.7]  | 1.09 [0.7-1.8]  |
| Extremely poor | 0.85 [0.5-1.4]  | 1.09 [0.6-1.9]  | 1.53 [0.9-2.6]  | 1.68 [1.0-2.9]  | 1.23 [0.7-2.1]  | 1.42 [0.8-2.5]  |
| ***Creche*** |  |  |  |  |  |  |
| No crèche | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Attended crèche | **1.85\* [1.1-3.2]**  | **1.74\* [1.0-3.0]**  | 0.86 [0.5-1.5]  | 0.75 [0.4-1.3]  | 1.30 [0.8-2.2]  | 1.13 [0.6-2.0]  |
| ***MC-Homeb (Current)*** |  |  |  |  |  |  |
| Low Total | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Total | 0.98 [0.7-1.3]  | 0.90 [0.7-1.2]  | **1.39\* [1.1-1.8]**  | **1.36\* [1.0-1.8]**  | **1.35\* [1.0-1.8]**  | **1.35\* [1.0-1.8]**  |
| ***Maternal mental health (Current)*** |  |  |  |  |  |  |
| No mental disorders | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Depression or anxiety or alcohol use | 1.00 [0.6-1.6]  | 1.02 [0.6-1.7]  | 1.04 [0.6-1.7]  | 1.07 [0.6-1.8]  | 1.05 [0.6-1.7]  | 1.05 [0.6-1.8]  |
| ***Parenting stress (Current)*** |  |  |  |  |  |  |
| Parenting stress ≤ 90 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Parenting stress ≥ 90 | 0.96 [0.6-1.4]  | 1.01 [0.7-1.6]  | 0.89 [0.6-1.3]  | 0.84 [0.5-1.3]  | 0.92 [0.6-1.4]  | 0.89 [0.6-1.4]  |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the confidence intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*ORs based on bivariate logistic regression of the outcome on the covariate. AORs based on multivariate logistic regression on the outcomes including all covariates*

*Animal Sorting: measures inhibition, planning, cognitive flexibility*

*Auditory Attention: measures vigilance, selective/ sustained auditory attention*

*Response Set: measures inhibition of previously learned stimuli*

Emotional and behavioural problems

Being born in an urban environment, and having a primary caregiver with high parenting stress, were associated with more emotional and behavioural problems (higher scores on the Internalising and Externalising sub-scales and Total score) (Total scores: urban: aOR 1.62 [95% CI 1.2-2.2] p=0.01) parenting stress: aOR 7.04 [95% CI 4.2-11.9] p<0.001). Children whose caregiver had a current mental health disorder were more likely to score above the mean for Internalising (aOR 1.92 [95% CI 1.1-3.4] p=0.03) and Total scores (aOR 2.44 [95% CI 1.3-4.6] p=0.01) (Table 4). Boys were more likely to score above the mean for Internalising (aOR 1.53 [95% CI 1.1-2.0], p=0.01) whilst children who attended a crèche were approximately twice as likely to score above the mean in Externalising (aOR 2.15 [95% CI 1.2-3.9], p=0.01) and Total scores (aOR 1.96 [95% CI 1.0-3.8], p=0.05). EBF and mother’s antenatal or current HIV status were not significantly associated with Externalising, Internalising or Total CBCL score.

Table 4 Factors associated with children's emotional and behavioural outcomes measured by the Child Behaviour Checklist (CBCL)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **CBCL Internalising (N=823)** | **CBCL Externalising(N=823)** | **CBCL Total (N=823)** |
|  | **OR [CI]**  | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]**  | **OR [CI]**  | **AOR [CI]**  |
| ***Sex*** |  |  |  |  |  |  |
| Female | 1.00  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Male | **1.59\*\* [1.2-2.1]** | **1.53\*\* [1.1-2.0]**  | 1.13 [0.9-1.5]  | 1.03 [0.8-1.4]  | **1.42\* [1.1-1.9]**  | 1.33 [1.0-1.8]  |
| ***Child Age (Current)*** |  |  |  |  |  |  |
| 8 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 9 years | 0.87 [0.5-1.7]  | 0.81 [0.4-1.6]  | 1.00 [0.5-2.0]  | 0.97 [0.5-2.1]  | 1.04 [0.5-2.0]  | 1.04 [0.5-2.0]  |
| 10 years | 0.74 [0.4-1.4]  | 0.70 [0.4-1.4]  | 0.90 [0.4-1.8]  | 0.97 [0.5-2.1]  | 0.90 [0.5-1.8]  | 0.99 [0.5-2.0]  |
| 11 years | 0.66 [0.3-1.4]  | 0.72 [0.3-1.7]  | 0.99 [0.4-2.2]  | 1.35 [0.6-3.3]  | 0.98 [0.5-2.2]  | 1.38 [0.6-3.3]  |
| ***Mother's Age (at birth)*** |  |  |  |  |  |  |
| Less than 20 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 20-29 years | 0.91 [0.6-1.3]  | 0.83 [0.5-1.3]  | 0.86 [0.6-1.2]  | 0.80 [0.5-1.2]  | 1.02 [0.7-1.5]  | 0.95 [0.6-1.5]  |
| 30+ years | 0.88 [0.6-1.3]  | 0.90 [0.5-1.7]  | 0.84 [0.6-1.2]  | 0.85 [0.5-1.6]  | 0.99 [0.7-1.5]  | 1.15 [0.6-2.1]  |
| ***Maternal IQ (Current)a*** |  |  |  |  |  |  |
| Low Raven’s | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Raven’s | 1.05 [0.8-1.4]  | 1.01 [0.7-1.4]  | 1.15 [0.9-1.5]  | 1.20 [0.9-1.7]  | 1.18 [0.9-1.6]  | 1.24 [0.9-1.7]  |
| ***Mother's Education (at birth)*** |  |  |  |  |  |  |
| None | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Primary | 1.24 [0.7-2.2]  | 1.11 [0.6-2.0]  | 1.12 [0.6-2.0]  | 1.02 [0.5-1.9]  | 1.06 [0.6-1.9]  | 0.89 [0.5-1.7]  |
| Some secondary | 1.23 [0.7-2.2]  | 1.08 [0.6-2.0]  | 1.18 [0.7-2.1]  | 0.93 [0.5-1.8]  | 1.13 [0.6-2.0]  | 0.83 [0.4-1.7]  |
| Completed secondary/post | 1.50 [0.8-2.8]  | 1.34 [0.7-2.7]  | 1.05 [0.6-2.0]  | 0.84 [0.4-1.7]  | 1.20 [0.6-2.2]  | 0.83 [0.4-1.8]  |
| ***Birthweight*** |  |  |  |  |  |  |
| Low Birthweight | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Normal Birthweight | 0.86 [0.5-1.3]  | 0.80[0.5-1.3] | 0.83[0.5-1.3] | 0.83[0.5-1.4] | 0.75[0.5-1.2] | 0.69[0.4-1.1] |
| ***Exclusive Breastfeeding*** |  |  |  |  |  |  |
| 0-1 months | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2-5 months | 1.04 [0.7-1.7]  | 1.20 [0.7-2.0]  | 0.71 [0.4-1.2]  | 0.69 [0.4-1.2]  | 0.81 [0.5-1.3]  | 0.93 [0.6-1.6] |
| 6 months | 0.94 [0.6-1.4]  | 1.12 [0.7-1.8]  | 0.81 [0.5-1.3]  | 0.81 [0.5-1.3]  | 0.75 [0.5-1.2]  | 0.87 [0.5-1.4]  |
| ***Birth order (Birth)*** |  |  |  |  |  |  |
| Birth order 1-2 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Birth order 3-4 | 0.96 [0.7-1.3]  | 0.97 [0.6-1.5]  | 0.96 [0.7-1.3]  | 0.98 [0.6-1.5]  | 0.93 [0.7-1.3]  | 0.86 [0.6-1.3]  |
| Birth order 5+ | 0.83 [0.6-1.2]  | 0.83 [0.5-1.5]  | 0.85 [0.6-1.2]  | 0.81 [0.4-1.5]  | 0.80 [0.6-1.2]  | 0.66 [0.4-1.2]  |
| ***Mother's HIV status*** |  |  |  |  |  |  |
| Negative | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Positive pregnancy | 0.96 [0.7-1.3]  | 0.88 [0.6-1.3]  | 0.97 [0.7-1.3]  | 0.82 [0.6-1.2]  | 1.04 [0.8-1.4]  | 0.84 [0.6-1.2]  |
| Positive since pregnancy | 1.06 [0.7-1.5]  | 0.93 [0.6-1.4]  | 1.12 [0.8-1.6]  | 0.91 [0.6-1.4]  | 1.10 [0.8-1.6]  | 0.91 [0.6-1.4]  |
| ***Residence (at birth)*** |  |  |  |  |  |  |
| Rural  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Urban  | **1.50\*\* [1.1-2.0]**  | **1.45\* [1.1-2.0]**  | **1.35\* [1.0-1.8]**  | **1.39\* [1.0-1.9]**  | **1.56\*\* [1.2-2.1]**  | **1.62\*\* [1.2-2.2]**  |
| ***Income provider (at birth)*** |  |  |  |  |  |  |
| Other | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Mother | 1.12 [0.7-1.8]  | 1.07 [0.6-1.8]  | 1.21 [0.7-2.0]  | 1.18 [0.7-2.1]  | 1.51 [0.9-2.4]  | 1.41 [0.8-2.4]  |
| ***Owns fridge (at birth)*** |  |  |  |  |  |  |
| Fridge No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Fridge Yes | 1.07 [0.8-1.4]  | 1.07 [0.8-1.5]  | 1.00 [0.8-1.3]  | 0.99 [0.7-1.4]  | 1.01 [0.8-1.3]  | 0.94 [0.7-1.3]  |
| ***Perception wealth(Current)*** |  |  |  |  |  |  |
| Very comfortable | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Getting by | 0.96 [0.6-1.5]  | 1.04 [0.6-1.8]  | 1.07 [0.7-1.7]  | 1.18 [0.7-2.0]  | 0.68 [0.4-1.1]  | 0.74 [0.4-1.2]  |
| Extremely poor | 1.21 [0.7-2.0]  | 1.28 [0.7-2.3]  | 1.26 [0.8-2.1]  | 1.26 [0.7-2.2]  | 0.84 [0.5-1.4]  | 0.82 [0.5-1.5]  |
| ***Creche*** |  |  |  |  |  |  |
| No crèche | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Attended crèche | 0.94 [0.6-1.6]  | 1.07 [0.6-1.9]  | 1.59 [0.9-2.7]  | **2.15\* [1.2-3.9]**  | 1.44 [0.8-2.5]  | **1.96\* [1.0-3.8]**  |
| ***MC-Homeb(Current)*** |  |  |  |  |  |  |
| Low Total | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Total | 1.28 [1.0-1.7]  | 1.3 [1.0-1.7]  | 1.11 [0.8-1.5]  | 1.10 [0.8-1.5]  | 1.30 [1.0-1.7]  | 1.26 [0.9-1.7]  |
| ***Maternal mental health (Current)*** |  |  |  |  |  |  |
| No mental disorders | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Depression or anxiety or alcohol use | **2.62\*\*\* [1.6-4.4]**  | **1.92\* [1.1-3.4]**  | **2.29\*\* [1.4-3.8]**  | 1.58 [0.9-2.8]  | **3.55\*\*\* [2.1-6.0]**  | **2.44\*\* [1.3-4.6]**  |
| ***Parenting stress (Current)*** |  |  |  |  |  |  |
| Parenting stress ≤ 90 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Parenting stress ≥ 90 | **3.79\*\*\* [2.4-6.0]**  | **3.33\*\*\* [2.1-5.3]**  | **5.75\*\*\* [3.6-9.2]**  | **5.93\*\*\* [3.5-9.9]**  | **7.22\*\*\* [4.4-11.8]**  | **7.04\*\*\* [4.2-11.9]**  |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the confidence intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*ORs based on bivariate logistic regression of the outcome on the covariate. AORs based on multivariate logistic regression on the outcomes including all covariates*

*The Child Behaviour Check List (CBCL) includes 120-items in two subscales: ‘Internalising disorders’ and ‘Externalising disorders’, and a composite Total score. A high score indicates more problems.*

Exploring the six DSM disorders (Table 5), EBF was significantly associated with lower scores (fewer problems) for conduct disorders. Those who were EBF for six months compared to one month or less were approximately half as likely to score above the mean for conduct disorders (aOR 0.44 [95% CI 0.3-0.7] p<0.01). Caregiver mental health and stress were associated with increases in all six disorders. Urban residence was associated with increases in somatic, Attention Deficit Hyperactivity Disorder (ADHD) and oppositional problems. Boys were less likely to be anxious (aOR 0.64 [95% CI 0.5-0.9] p<0.01) but more likely to have somatic (aOR 1.34 [95% CI 1.0-1.8], p=0.05) or oppositional disorders (aOR 1.52 [95% CI 1.1-2.2], p=0.02).

**Table 5:** Child Diagnostic and Statistical Manual (DSM) Disorders measured by Children Behaviour Checklist (overall cohort of girls and boys)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Affective (N=823)****AOR [CI]** | **Anxious (N=823)****AOR [CI]** | **Somatic (N=823)****AOR [CI]** | **ADHD (N=823)****AOR [CI]** | **Oppositional (N=823)****AOR [CI]** | **Conduct (N=823)****AOR [CI]** |
| ***Child Sex*** |  |  |  |  |  |  |
| Female | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Male | 1.09 [0.7-1.5] | **0.64\*\* [0.5 -0.9]** | **1.34\* [1.0-1.8]** | 1.13 [0.8-1.6] | **1.52\* [1.1-2.2]** | 1.15 [0.8-1.6] |
| ***Child Age (Current)*** |  |  |  |  |  |  |
| 8 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 9 years | 0.86 [0.4-2.0] | 1.39 [0.6-3.1] | 0.60 [0.3-1.2] | 0.73 [0.3-1.7] | 1.07 [0.5-2.4] | 0.90 [0.4-2.1] |
| 10 years | 0.76 [0.3-1.9] | 1.49 [0.7-3.4] | 0.54 [0.3-1.1] | 0.65 [0.3-1.5] | 1.39 [0.6-3.2] | 1.07 [0.5-2.5] |
| 11 years | 0.97 [0.3-2.8] | 1.86 [0.7-4.7] | 0.93 [0.4-2.1] | 1.50 [0.5-4.2] | 1.79 [0.6-5.0] | 1.29 [0.5-3.5] |
| ***Mother's Age (at birth)*** |  |  |  |  |  |  |
| Less than 20 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 20-29 years | 1.04 [0.6-1.7] | 0.74 [0.5-1.2] | 0.90 [0.6-1.4] | 1.28 [0.8-2.2] | 1.12 [0.7-1.9] | 1.07 [0.7-1.7] |
| 30+ years | 1.17 [0.6-2.3] | 0.73 [0.4-1.4] | 0.98 [0.5-1.8] | 0.99 [0.5-2.1] | 1.17 [0.6-2.5] | 1.07 [0.5-2.1] |
| ***Maternal IQ (Current)a*** |  |  |  |  |  |  |
| Low Raven’s | 1.00  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Raven’s | 0.80 [0.6-1.2] | 1.03 [0.7-1.4] | 0.97 [0.7-1.3] | **1.49\* [1.0-2.2]** | 1.05 [0.7-1.5] | 1.19 [0.8-1.7] |
| ***Mother's Education (at birth)*** |  |  |  |  |  |  |
| None | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Primary | 0.83 [0.4-1.8] | 0.99 [0.5-1.8] | 0.77 [0.4-1.4] | 1.40 [0.7-3.0] | 1.13 [0.5-2.5] | 0.93 [0.5-1.9] |
| Some secondary | 0.81 [0.4-1.8] | 0.81 [0.4-1.6] | 0.77 [0.4-1.5] | 0.87 [0.4-2.0] | 1.12 [0.5-2.6] | 0.74 [0.3-1.6] |
| Completed secondary/post | 0.49 [0.20-1.2] | 0.91 [0.4-1.9] | 0.82 [0.4-1.7] | 0.61 [0.3-1.5] | 1.25 [0.5-3.0] | **0.40\* [0.1-0.9]** |
| ***Birthweight*** |  |  |  |  |  |  |
| Low Birthweight | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Normal Birthweight | 0.66 [0.4-1.1] | 0.70 [0.4-1.1] | 0.88 [0.6-1.4] | 0.65 [0.4-1.1] | 0.68 [0.4-1.2] | 0.72 [0.4-1.2] |
| ***Exclusive Breastfeeding*** |  |  |  |  |  |  |
| 0-1 months | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2-5 months | 0.94 [0.5-1.7] | 0.92 [0.5-1.6] | 1.18 [0.7-2.0] | 0.81 [0.4-1.5] | 0.76 [0.4-1.4] | **0.35\*\*\* [0.2-0.6]** |
| 6 months | 0.94 [0.5-1.7] | 0.90 [0.5-1.5] | 1.11 [0.7-1.8] | 0.94 [0.5-1.6] | 0.89 [0.5-1.6] | **0.44\*\* [0.3-0.7]** |
| ***Birth order (Birth)*** |  |  |  |  |  |  |
| Birth order 1-2 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Birth order 3-4 | 0.64 [0.4-1.1] | 0.84 [0.5-1.3] | 1.00 [0.7-1.5] | 0.65 [0.4-1.0] | 0.85 [0.5-1.4] | 0.71 [0.4-1.1] |
| Birth order 5+ | 0.54 [0.3-1.1] | 0.80 [0.4-1.5] | 0.93 [0.5-1.7] | 0.67 [0.3-1.4] | 0.78 [0.8-1.6] | **0.44\* [0.2-0.9]** |
| ***Mother's HIV status*** |  |  |  |  |  |  |
| Negative | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Positive pregnancy | 0.97 [0.6-1.5] | 0.90 [0.6-1.3] | 0.86 [0.6-1.2] | 0.86 [0.6-1.3] | **0.58\* [0.4-0.9]** | 0.74 [0.5-1.1] |
| Positive since pregnancy | 1.32 [0.8-2.1] | 1.01 [0.7-1.5] | 0.75 [0.5-1.1] | 1.00 [0.6-1.6] | 0.70 [0.4-1.2] | 0.68 [0.4-1.1] |
| ***Residence (at birth)*** |  |  |  |  |  |  |
| Rural  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Urban  | 1.13 [0.8-1.7] | 1.21 [0.9-1.7] | **1.46\* [1.0-2.0]** | 1.44 [1.0-2.1] | **1.57\* [1.1-2.3]** | 1.26 [0.9-1.8] |
| ***Income provider (at birth)*** |  |  |  |  |  |  |
| Other | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Mother | 0.73 [0.4-1.4] | 0.93 [0.5-1.7] | 1.06 [0.6-1.8] | 1.66 [0.9-3.0] | 0.80 [0.4-1.6] | 0.98 [0.5-1.9] |
| ***Owns fridge(at birth)*** |  |  |  |  |  |  |
| Fridge No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Fridge Yes | 0.81 [06-1.2] | 0.92 [0.7-1.3] | 0.82 [0.6-1.1] | 1.04 [0.7-1.5] | 0.91 [0.6-1.3] | 1.01 [0.7-1.4] |
| ***Perception wealth(Current)*** |  |  |  |  |  |  |
| Very comfortable | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Getting by | 1.15 [0.6-2.2] | 0.93 [0.5-1.6] | 1.20 [0.7-2.0] | 0.65 [0.4-1.2] | 0.68 [0.4-1.2] | 0.89 [0.5-1.6] |
| Extremely poor | 1.38 [0.7-2.8] | 1.55 [0.9-2.8] | 1.22 [0.7-2.2] | 0.88 [0.5-1.7] | 0.75 [0.4-1.4] | 1.02 [0.5-1.9] |
| ***Creche*** |  |  |  |  |  |  |
| No creche | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Attended creche | 1.25 [0.6-2.5] | 0.98 [0.5-1.8] | 1.01 [0.6-1.8] | 1.97 [0.9-4.3] | **3.42\*\* [1.5-8.0]** | 1.34 [0.7-2.6] |
| ***MC-Homeb(Current)*** |  |  |  |  |  |  |
| Low Total | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Total | **1.54\* [1.1-2.2]** | 1.24 [0.9-1.7] | 1.26 [0.9-1.7] | 0.79 [0.6-1.1] | 1.17 [0.8-1.7] | 0.87 [0.6-1.2] |
| ***Maternal mental health (Current)*** |  |  |  |  |  |  |
| No mental disorders | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Depression or anxiety or alcohol use | **1.97\* [1.1-3.6]** | **2.03\*\* [1.2-3.4]** | **1.93\* [1.1-3.3]** | 1.40 [0.8-2.6] | **1.95\* [1.1-3.6]** | 1.77 [1.0-3.2] |
| ***Parenting stress (Current)*** |  |  |  |  |  |  |
| Parenting stress ≤ 90 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Parenting stress ≥ 90 | **5.39\*\*\* [3.4-8.5]** | **2.23\*\*\* [1.4-3.5]** | **2.08\*\* [1.4-3.2]** | **4.85\*\*\* [3.1-7.7]** | **4.68\*\*\* [3.0-7.4]** | **5.80\*\*\* [3.7-9.1]** |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the Confidence Intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*ORs based on bivariate logistic regression of the outcome on the covariate. AORs based on multivariate logistic regression on the outcomes including all covariatesThe Child Behaviour Check List (CBCL) scores for six Diagnostic and Statistical Manual (DSM) disorders: Affective, Anxious, Somatic, Attention Deficit Hyperactivity Disorder, Oppositional and Conduct disorders*

Outcomes stratified by sex (Tables 6-9)

Contrary to the finding in the overall cohort, boys, but not girls, who were EBF for more than one month were twice as likely than those EBF for a very short period to score above the mean for Learning Ability (aOR 2.07 [95% CI 1.0-4.3] p=0.05) and half as likely to score above the mean for Externalising problems (aOR 0.48 [95% CI 0.2-1.0] p=0.05) (Tables 7 and 9). However, girls who were EBF for less than one month were more likely to score above average on Auditory Attention compared to those EBF for longer. The finding of an association between maternal cognitive ability and improved performance on all four cognitive sub-scales in the overall cohort, held for boys, but not girls. Boys whose mother’s cognitive ability was above the median score (Standard Raven’s Progressive Matrix) were twice as likely to score above average for the cognitive sub-scales (e.g. Planning sub-scale aOR 2.79 [95% CI 1.8-4.4] p=<0.001). Maternal HIV status was not significantly associated with cognitive development, executive function or emotional-behavioural problems overall. However, boys whose mothers became infected with HIV after pregnancy were more likely to score below the mean on the Planning Ability sub-scale than those whose mothers remained HIV-negative (aOR 0.55 [95% CI 0.3-1.0] p=0.05). Boys born to HIV-positive mothers, compared to HIV-negative mothers, were more likely to score above average for reasoning and language ability (Riddles sub-test) (aOR 1.92 [95% CI 1.1-3.3] p=0.02). For girls, being born to an HIV-positive mother was associated with scoring below the mean for Planning Ability (aOR 0.53 [95% CI 0.3-0.9] p=0.01), and below the mean (fewer problems) for Externalising (aOR 0.56 [95% CI 0.2-0.9] p=0.03) and Total (aOR 0.56 [95% CI 0.3-1.0] p=0.03) CBCL scores.

Girls, but not boys, with a normal birth-weight were significantly more likely to score above the mean for Learning Ability (aOR 2.40 [95% CI 1.2-5.0] p=0.02) and Planning Ability (aOR 2.04 [95% CI 1.1-3.9] p=0.03), and below the mean (fewer problems) for Total Child Behaviour Check List score (aOR 0.42 [95% CI 02.-0.9] p=0.02). Boys of birth order of five or more were less likely than first-borns to score above average on Animal Sorting (inhibition, planning, cognitive flexibility) (aOR 0.40 [95% CI 0.2-1.0] p=0.04); girls of birth order of five or more were significantly more likely to have a lower Externalising CBCL score (aOR 0.38 [95% CI 0.2-0.9] p=0.03).

In this stratified analysis, the associations between maternal education and cognitive outcomes, and HOME scores and executive function, held for girls but not boys. Likewise, girls were approximately three times more likely to score above the median for higher emotional-behavioural problems if their mothers had a mental health problem (Total CBCL aOR 3.28 [95% CI 1.4-8.0] p=0.01), or high parenting stress (Total CBCL 4.63 [2.1-10.1] p<0.001).

In the full model interactions between sex and EBF were significant for Conduct (p=0.02) and CBCL Internalising (p=0.02) outcomes, and marginally for Learning (p=0.07) and Auditory Attention (p=0.08).

In summary, while duration of EBF was not associated with child cognitive development or executive function in the overall sample (including girls and boys), it was associated with fewer conduct disorders, and, when stratified by sex, there was weak evidence of improved cognitive development in boys.

**Table 6 Girls:** Factors associated with children's cognitive and executive function outcomes measured by the Kauffman Assessment Battery (KABC-II) and Developmental Neuropsychological Assessment (NEPSY)

|  |  |  |
| --- | --- | --- |
|  | **Cognitive Assessment** | **Executive Function Assessment** |
| **Sequential** | **Planning** | **Learning** | **Simultaneous** | **Riddles** | **Animal sorting** | **Auditory attention** | **Response set** |
|  | **AOR [CI]** | **AOR [CI]** | **AOR [CI]** | **AOR [CI]** | **AOR [CI]** | **AOR [CI]** | **AOR [CI]** | **AOR [CI]** |
| ***Child Age (Current)*** |  |  |  |  |  |  |  |  |
| 8 years | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 9 years | 0.94 [0.4-2.3] | 0.83 [0.4-1.8] | 0.85 [0.4-2.0] | 0.65 [0.3-1.6] | 2.13 [0.8-5.5] | 0.77 [0.3-2.0] | 2.23 [0.9-5.9] | 2.21 [0.8-5.9] |
| 10 years | 0.82 [0.3-2.1] | 1.02 [0.4-2.3] | 0.95 [0.4-2.3] | 0.43 [0.2-1.1] | 1.54 [0.6-4.1] | 0.68 [0.2-1.9] | **4.00\*\* [1.5-10.8]** | 2.64 [1.0-7.2] |
| 11 years | 0.95 [0.3-3.0] | 0.94 [0.3-2.8] | 1.04 [0.3-3.2] | 0.74 [0.2-2.2] | 0.91 [0.3-3.1] | 0.99 [0.3-3.4] | 1.84 [0.6-5.8] | 0.77 [0.2-2.5] |
| ***Mother's Age (at birth)*** |  |  |  |  |  |  |  |  |
| Less than 20 years | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 20-29 years | 0.99[0.6-1.8] | 0.77 [0.4-1.4] | 0.97 [0.5-1.7] | 1.25 [0.7-2.2] | 1.07 [0.6-2.0] | 1.51 [0.8-2.7] | 1.78 [1.0-3.2] | **0.46\* [0.2-0.9]** |
| 30+ years | 1.67 [0.7-3.8] | 0.94 [0.4-2.1] | 2.17 [1.0-4.9] | 1.06 [0.5-2.4] | 1.42 [0.6-3.3] | 0.92 [0.4-2.1] | 2.01 [0.9-4.6] | 0.54 [0.2-1.4] |
| ***Maternal IQ (Current)a*** |  |  |  |  |  |  |  |  |
| Low Raven’s | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| High Raven’s | 1.15 [0.7-1.8] | 1.07 [0.7-1.7] | 1.31 [0.8-2.0] | 0.96 [0.6-1.5] | 1.23 [0.8-1.9] | 0.88 [0.6-1.4] | 1.06 [0.7-1.7] | 1.05 [0.7-1.7] |
| ***Mother's Education (at birth)*** |  |  |  |  |  |  |  |  |
| None | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Primary | 0.79 [0.4-1.7] | 0.85 [0.4-1.9] | 1.15 [0.5-2.7] | 1.54 [0.7-3.5] | 0.73 [0.3-1.7] | 0.93 [0.4-2.0] | 0.64 [0.3-1.5] | 0.76 [0.3-1.7] |
| Some secondary | 0.99 [0.4-2.2] | 2.02 [0.9-4.7] | 1.45 [0.6-3.5] | **2.65\* [1.1-6.3]** | 1.36 [0.6-3.3] | 1.03 [0.5-2.3] | 1.42 [0.6-3.3] | 1.98 [0.8-4.8] |
| Completed secondary/post | 1.36 [0.5-3.4] | 2.39 [0.9-6.2] | 2.02 [0.8-5.3] | **4.10\*\* [1.6-10.8]** | 2.47 [0.9-6.5] | 1.72 [0.7-4.4] | 0.91 [0.4-2.4] | 1.23 [0.5-3.3] |
| ***Birthweight*** |  |  |  |  |  |  |  |  |
| Low Birthweight | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Normal Birthweight | 1.39 [0.7-2.7] | **2.04\* [1.1-3.9]** | **2.40\* [1.2-5.0]** | 1.82 [0.9-3.5] | 1.17 [0.5-2.6] | 1.42 [0.7-2.8] | 1.13 [0.6-2.1] | 1.36 [0.7-2.7] |
| ***Exclusive Breastfeeding*** |  |  |  |  |  |  |  |  |
| 0-1 months | 1 | 1 | 1 | 1  | 1 | 1  | 1 | 1 |
| 2-5 months | 1.34 [0.6-2.8] | 0.70 [0.3-1.5] | 0.57 [0.3-1.2] | 1.10 [0.5-2.3] | 1 [0.5-2.2] | 1.16 [0.5-2.6] | **0.35\*\* [0.2-0.8]** | 1.06 [0.5-2.4] |
| 6 months | 1.69 [0.8-3.5] | 0.49 [0.2-1.0] | 0.77 [0.4-1.6] | 1.07 [0.5-2.2] | 0.90 [0.4-2.0] | 1.53 [0.7-3.3] | **0.46\* [0.2-1.0]** | 1.15 [0.5-2.6] |
| ***Birth order (Birth)*** |  |  |  |  |  |  |  |  |
| Birth order 1-2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Birth order 3-4 | 0.74 [0.4-1.3] | 0.97 [0.5-1.7] | 0.75 [0.4-1.3] | 1.25 [0.7-2.2] | 1.13 [0.6-2.1] | 1.23 [0.7-2.2] | 1.01 [0.6-1.8] | 1.37 [0.8-2.5] |
| Birth order 5+ | 0.62 [0.3-1.4] | 1.17 [0.51-2.6] | **0.40\* [0.2-0.9]** | 1.47 [0.6-3.4] | 0.98 [0.4-2.3] | 1.42 [0.6-3.2] | 1.61 [0.7-3.8] | 0.98 [0.4-2.4] |
| ***Mother's HIV status*** |  |  |  |  |  |  |  |  |
| Negative | 1 | 1 | 1 | 1 | 1 | 1  | 1 | 1 |
| Positive pregnancy | 0.96 [0.6-1.6] | **0.53\* [0.3-0.9]** | 1.05 [0.6-1.7] | 0.71 [0.4-1.1] | 0.89 [0.5-1.5] | 0.93 [0.6-1.5] | 0.86 [0.5-1.4] | 0.93 [0.6-1.6] |
| Positive since pregnancy | 0.79 [0.4-1.4] | 0.75 [0.4-1.4] | 0.82 [0.5-1.5] | 0.63 [0.3-1.2] | 1.13 [0.6-2.0] | 0.97 [0.6-1.7] | 0.90 [0.5-1.6] | 0.86 [0.4-1.6] |
| ***Residence (at birth)*** |  |  |  |  |  |  |  |  |
| Rural  | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Urban  | 1.41 [0.9-2.2] | 1.48 [0.9-2.3] | 1.10 [0.7-1.7] | 1.26 [0.8-2.0] | 1.59 [1.0-2.5] | 1.29 [0.8-2.0] | 0.85 [0.5-1.4] | 0.98 [0.6-1.6] |
| ***Income provider (at birth)*** |  |  |  |  |  |  |  |  |
| Other | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Mother | 0.93 [0.4-2.1] | 0.78 [0.3-1.8] | 1.07 [0.5-2.4] | 1.26 [0.5-2.9] | 1.30 [0.5-3.3] | 1.57 [0.7-3.6] | 0.45 [0.2-1.1] | 0.94 [0.4-2.2] |
| ***Owns fridge(at birth)*** |  |  |  |  |  |  |  |  |
| Fridge No | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Fridge Yes | 1.11 [0.7-1.7] | 1.37 [0.9-2.1] | 1.35 [0.9-2.1] | 1.46 [0.9-2.3] | 0.96 [0.7-1.5] | 1.09 [0.7-1.7] | 1.25 [0.8-2.0] | 1.52 [1.0-2.4] |
| ***Perception wealth(Current)*** |  |  |  |  |  |  |  |  |
| Very comfortable | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Getting by | 0.52 [0.2-1.0] | 0.81 [0.4-1.7] | 1.43 [0.7-3.0] | 1.44 [0.7-3.0] | 0.70 [0.3-1.4] | 0.99 [0.5-2.1] | 1.03 [0.5-2.2] | 1.07 [0.5-2.2] |
| Extremely poor | 0.61 [0.3-1.4] | 1.09 [0.4-2.4] | 1.18 [0.5-2.6] | 1.17 [0.5-2.6] | 0.64[0.3-1.4] | 0.73 [0.3-1.6] | 1.06 [0.5-2.4] | 1.43 [0.7-3.1] |
| ***Creche*** |  |  |  |  |  |  |  |  |
| No creche | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Attended creche | 1.17 [0.5-3.0] | 1.04 [0.4-2.6] | 1.01 [0.4-2.9] | 0.75 [0.3-2.0] | 0.66 [0.2-1.8] | 2.47 [0.9-6.5] | 0.42 [0.2-1.1] | 2.03 [0.7-5.9] |
| ***MC-Homeb(Current)*** |  |  |  |  |  |  |  |  |
| Low Total | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| High Total | 0.91 [0.6-1.4] | 0.95 [0.6-1.5] | 1.01 [0.6-1.6] | 0.89 [0.6-1.4] | 0.78 [0.5-1.2] | 0.85 [0.6-1.3] | **1.73\* [1.1-2.7]** | **1.69\* [1.1-2.6]** |
| ***Maternal mental health (Current)*** |  |  |  |  |  |  |  |  |
| No mental disorders | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Depression or anxiety or alcohol use | 2.08 [0.9-4.6] | 1.19 [0.6-2.5] | 0.60 [0.3-1.3] | 0.91 [0.4-2.0] | 0.68 [0.3-1.5] | 0.72 [0.3-1.6] | 1.18 [0.5-2.6] | 2.12 [0.9-4.7] |
| ***Parenting stress (Current)*** |  |  |  |  |  |  |  |  |
| Parenting stress ≤ 90 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Parenting stress ≥ 90 | 0.72 [0.4-1.4] | 0.76 [0.4-1.5] | 1.12 [0.5-2.3] | 1.08 [0.5-2.2] | 1.51 [0.8-3.0] | 1.31 [0.6-2.7] | 0.64 [0.3-1.2] | 0.66 [0.3-1.3] |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the Confidence Intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*AORs based on multivariate logistic regression on the outcomes including all covariates*

*Sequential Processing: measures audio and visual memory and memory span*

*Simultaneous Processing: measures spatial and visual perception, reasoning and maths ability*

*Learning ability: measures focused and selective attention, and ability to store auditory and visual stimuli simultaneously*

*Planning: measures decision making ability*

*Riddles: measures reasoning and language development*

*Animal Sorting: measures inhibition, planning, cognitive flexibility*

*Auditory Attention: measures vigilance, selective/ sustained auditory attention*

*Response Set: measures inhibition of previously learned stimuli*

**Table 7 Boys:** Factors associated with children's cognitive and executive function outcomes measured by the Kauffman Assessment Battery (KABC-II) and Developmental Neuropsychological Assessment (NEPSY)

|  |  |  |
| --- | --- | --- |
|  | **Cognitive Assessment** | **Executive Function Assessment** |
| **Sequential** | **Planning** | **Learning** | **Simultaneous** | **Riddles** | **Animal sorting** | **Auditory attention** | **Response set** |
|  | AOR [CI] | AOR [CI] | AOR [CI] | AOR [CI] | AOR [CI] | AOR [CI] | AOR [CI] | AOR [CI] |
| ***Child Age (Current)*** |  |  |  |  |  |  |  |  |
| 8 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 9 years | 1.32 [0.5-3.9] | 2.42 [0.8-7.5] | 1.56 [0.5-4.9] | 0.68 [0.2-2.5] | 0.37 [0.1-1.2] | 0.55 [0.2-1.8] | **12.69\* [1.7-95.3]** | 0.93 [0.3-2.8] |
| 10 years | 1.02 [0.3-3.0] | 1.87 [0.6-5.9] | 1.16 [0.4-3.7] | 0.56 [0.2-2.1] | **0.27\* [0.1-0.9]** | 0.57 [0.2-1.9] | **14.46\* [1.9-109.1]** | 0.62 [0.2-1.9] |
| 11 years | 0.77 [0.2-2.8] | 0.77 [0.2-3.0] | 1.25 [0.3-4.8] | 0.37 [0.1-1.6] | **0.14\*\* [0.0-0.6]** | 0.93 [0.2-3.7] | **6.74\* [0.8-56.9]** | 0.53 [0.1-1.9] |
| ***Mother's Age (at birth)*** |  |  |  |  |  |  |  |  |
| Less than 20 years | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 20-29 years | 1.16 [0.6-2.2] | 0.83 [0.4-1.6] | 1.37 [0.7-2.6] | 1.05 [0.6-1.9] | 1.07 [0.5-2.1] | **2.17\* [1.1-4.1]** | 0.60 [0.3-1.1] | 1.20 [0.6-2.3] |
| 30+ years | 1.54 [0.6-3.8] | 0.62 [0.2-1.6] | 1.61 [0.7-3.8] | 1.39 [0.6-3.3] | 0.92 [0.3-2.6] | **2.89\* [1.1-7.40]** | 0.97 [0.4-2.3] | 0.96 [0.4-2.2] |
| ***Maternal IQ (Current)a*** |  |  |  |  |  |  |  |  |
| Low Raven’s | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Raven’s | **1.77\* [1.1-2.8]** | **2.79\*\*\* [1.8-4.4]** | **2.05\*\* [1.3-3.2]** | **2.19\*\* [1.4-3.5]** | **2.20\*\* [1.4-3.6]** | 1.00 [0.6-1.6] | 1.06 [0.7-1.7] | 1.04 [0.7-1.6] |
| ***Mother's Education (at birth)*** |  |  |  |  |  |  |  |  |
| None | 1.00 | 1.00 | 1.00 | 1.00  | 1.00 | 1.00 | 1.00 | 1.00 |
| Primary | 1.24 [0.5-3.4] | 1.30 [0.5-3.3] | 0.71 [0.3-1.9] | 1.13 [0.4-2.9] | 1.19 [0.3-4.1] | 1.25 [0.5-3.3] | 0.43 [0.1-1.3] | 1.29 [0.5-3.4] |
| Some secondary | 1.51 [0.5-4.4] | 1.03 [0.4-2.8] | 0.72 [0.3-2.0] | 0.74 [0.3-2.1] | 1.57 [0.4-5.6] | 1.64 [0.6-4.6] | 0.55 [0.2-1.7] | 1.30 [0.5-3.7] |
| Completed secondary/post | 1.72 [0.5-5.4] | 1.31 [0.4-4.0] | 0.96 [0.3-2.9] | 1.25 [0.4-3.7] | 1.25 [0.3-4.8] | 1.47 [0.5-4.5] | 0.84 [0.3-2.8] | 1.52 [0.5-4.6] |
| ***Birthweight*** |  |  |  |  |  |  |  |  |
| Low Birthweight | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Normal Birthweight | 1.15 [0.5-2.4] | 0.97 [0.4-2.1] | 0.69 [0.3-1.4] | 1.09 [0.5-2.3] | 2.29 [0.8-6.2] | 1.68 [0.8-3.7] | 0.77 [0.4-1.6] | 0.93 [0.5-1.9] |
| ***Exclusive Breastfeeding*** |  |  |  |  |  |  |  |  |
| 0-1 months | 1.00  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2-5 months | 1.24 [0.6-2.5] | 1.08 [0.5-2.2] | **2.07\* [1.0-4.3]** | 1.52 [0.7-3.2] | 1.12 [0.5-2.4] | 1.14 [0.6-2.3] | 1.12 [0.6-2.2] | 1.27 [0.6-2.5] |
| 6 months | 0.90 [0.5-1.7] | 1.13 [0.6-2.1] | 1.87 [0.9-3.7] | 1.59 [0.8-3.1] | 1.58 [0.8-3.1] | 1.17 [0.6-2.3] | 0.85 [0.5-1.6] | 1.06 [0.6-2.0] |
| ***Birth order (Birth)*** |  |  |  |  |  |  |  |  |
| Birth order 1-2 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Birth order 3-4 | 1.03 [0.6-1.9] | 1.31 [0.7-2.5] | 0.97 [0.5-1.8] | 0.86 [0.5-1.6] | 1.45 [0.7-2.9] | 0.69 [0.4-1.3] | 1.46 [0.8-2.7] | 0.74 [0.4-1.4] |
| Birth order 5+ | 0.84 [0.4-2.0] | 1.89 [0.8-4.5] | 0.99 [0.4-2.3] | 1.21 [0.5-2.9] | 1.23 [0.4-3.4] | **0.40\* [0.2-1.0]** | 0.91 [0.4-2.1] | 0.94 [0.4-2.1] |
| ***Mother's HIV status*** |  |  |  |  |  |  |  |  |
| Negative | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Positive pregnancy | 1.27 [0.8-2.1] | 1.09 [0.7-1.8] | 1.26 [0.7-2.2] | 1.16 [0.7-1.9] | **1.92\* [1.1-3.3]** | 1.20 [0.7-2.0] | 1.02 [0.6-1.7] | 1.00 [0.6-1.7] |
| Positive since pregnancy | 0.84 [0.5-1.5] | **0.55\* [0.3-1.0]** | 1.57 [0.9-2.8] | 0.71 [0.4-1.3] | 0.88 [0.5-1.7] | 0.75 [0.4-1.4] | 0.78 [0.4-1.4] | 1.11 [0.6-2.0] |
| ***Residence (at birth)*** |  |  |  |  |  |  |  |  |
| Rural  | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Urban  | 1.14 [0.7-1.8] | 1.10 [0.7-1.7] | 1.12 [0.7-1.8] | 1.17 [0.7-1.8] | 0.91 [0.6-1.5] | 1.27 [0.8-2.0] | 0.95 [0.6-1.5] | 0.99 [0.6-1.6] |
| ***Income provider (at birth)*** |  |  |  |  |  |  |  |  |
| Other | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Mother | 0.75 [0.4-1.5] | 0.62 [0.3-1.2] | 0.72 [0.3.-1.5] | 1.36 [0.7-2.8] | 0.87 [0.4-1.9] | 1.96 [1.0-4.0] | 1.43 [0.7-3.0] | 1.03 [0.5-2.1] |
| ***Owns fridge*** |  |  |  |  |  |  |  |  |
| Fridge No | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Fridge Yes | 0.95 [0.6-1.5] | 0.97 [0.6-1.5] | 1.04 [0.7-1.6] | 0.87 [0.6-1.4] | 1.56 [1.0-2.5] | 1.31 [0.8-2.1] | 1.32 [0.8-2.1] | 0.74 [0.5-1.2] |
| ***Perception wealth(Current)*** |  |  |  |  |  |  |  |  |
| Very comfortable | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Getting by | 0.96 [0.4-2.1] | 0.83 [0.4-1.8] | 0.77 [0.4-1.5] | 0.72 [0.3-1.6] | 0.88 [0.4-1.9] | 1.40 [0.7-2.9] | 1.49 [0.7-3.1] | 1.09 [0.5-2.2] |
| Extremely poor | 1.00 [0.4-2.3] | 0.72 [0.3-1.6] | 0.74 [0.3-1.5] | 0.82 [0.3-1.9] | 0.70 [0.3-1.6] | 1.69 [0.7-3.7] | **2.81\* [1.2-6.3]** | 1.41 [0.6-3.1] |
| ***Creche*** |  |  |  |  |  |  |  |  |
| No creche | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Attended creche | **2.74\*\* [1.3-5.9]** | 1.23 [0.6-2.6] | 0.91 [0.5-1.8] | 1.12 [0.6-2.2] | 0.93 [0.4-2.0] | 1.73 [0.9-3.5] | 0.97 [0.5-2.0] | 0.91 [0.5-1.8] |
| ***MC-Homeb(Current)*** |  |  |  |  |  |  |  |  |
| Low Total | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| High Total | 0.96 [0.6-1.5] | 1.32 [0.9-2.0] | 1.39 [0.9-2.1] | 1.37 [0.9-2.1] | 1.00 [0.6-1.6] | 0.84 [0.5-1.3] | 1.08 [0.7-1.7] | 1.11 [0.7-1.7] |
| ***Maternal mental health(Current)*** |  |  |  |  |  |  |  |  |
| No mental disorders | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Depression or anxiety or alcohol use | 1.32 [0.6-2.9] | 0.94 [0.4-2.1] | 0.71 [0.3-1.5] | 0.64 [0.3-1.3] | 0.79 [0.4-1.8] | 1.44 [0.7-2.8] | 1.03 [0.5-2.2] | 0.55 [0.3-1.1] |
| ***Parenting stress(Current)*** |  |  |  |  |  |  |  |  |
| Parenting stress ≤ 90 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Parenting stress ≥ 90 | 1.14 [0.7-1.9] | 0.73 [0.4-1.3] | 0.67 [0.4-1.2] | 0.71 [0.4-1.2] | 0.96 [0.5-1.8] | 0.90 [0.50-1.6] | 1.00 [0.6-1.7] | 0.95 [0.6-1.6] |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the Confidence Intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*AORs based on multivariate logistic regression on the outcomes including all covariates*

*Sequential Processing: measures audio and visual memory and memory span*

*Simultaneous Processing: measures spatial and visual perception, reasoning and maths ability*

*Learning ability: measures focused and selective attention, and ability to store auditory and visual stimuli simultaneously*

*Planning: measures decision making ability*

*Riddles: measures reasoning and language development*

*Animal Sorting: measures inhibition, planning, cognitive flexibility*

*Auditory Attention: measures vigilance, selective/ sustained auditory attention*

*Response Set: measures inhibition of previously learned stimuli*

Table 8 Girls: Factors associated with children's emotional and behavioural outcomes measured by the Child Behaviour Checklist (CBCL)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **CBCL Internalising** | **CBCL externalising** | **CBCL total** |
|  | AOR [CI]  | AOR [CI] | AOR [CI]  |
| ***Child Age (Current)*** |  |  |  |
| 8 years | 1 | 1 | 1 |
| 9 years | 1.14 [0.5-2.9] | 1.20 [0.4-3.3] | 1.52 [0.6-4.2] |
| 10 years | 0.95 [0.4-2.5] | 1.33 [0.5-3.8] | 1.52 [0.5-4.3] |
| 11 years | 0.99 [0.3-3.2] | 1.80 [0.5-6.2] | 1.98 [0.6-7.0] |
| ***Mother's Age (at birth)*** |  |  |  |
| Less than 20 years | 1 | 1 | 1 |
| 20-29 years | 0.69 [0.4-1.3] | 0.88 [0.5-1.6] | 0.81 [0.4-1.5] |
| 30+ years | 1.21 [0.5-2.9] | 1.50 [0.6-3.5] | 1.40 [0.6-3.3] |
| ***Maternal IQ (Current)a*** |  |  |  |
| Low Raven’s | 1 | 1 | 1 |
| High Raven’s | 0.93 [0.6-1.5] | 1.39 [0.9-2.2] | 1.21 [0.8-1.9] |
| ***Mother's Education (at birth)*** |  |  |  |
| None | 1 | 1 | 1 |
| Primary | 1.37 [0.6-3.3] | 1.42 [0.6-3.3] | 1.99 [0.7-5.6] |
| Some secondary | 1.23 [0.5-3.0] | 1.22 [0.5-3.0] | 1.96 [0.7-5.7] |
| Completed secondary/post | 1.90 [0.7-5.1] | 1.51 [0.6-4.1] | 2.70 [0.9-8.6] |
| ***Birthweight*** |  |  |  |
| Low Birthweight | 1 | 1 | 1 |
| Normal Birthweight | 0.66 [0.4-1.2] | 0.62 [0.3-1.2] | **0.42\* [0.2-0.9]** |
| ***Exclusive Breastfeeding*** |  |  |  |
| 0-1 months | 1 | 1 | 1 |
| 2-5 months | 1.95 [0.9-4.4] | 1.13 [0.5-2.5] | 1.51 [0.7-3.4] |
| 6 months | 1.96 [0.9-4.3] | 1.37 [0.6-3.0] | 1.35 [0.6-3.0] |
| ***Birth order (Birth)*** |  |  |  |
| Birth order 1-2 | 1 | 1  | 1 |
| Birth order 3-4 | 0.92 [0.5-1.7] | 0.85 [0.5-1.6] | 0.84 [0.4-1.6] |
| Birth order 5+ | 0.74 [0.3-1.8] | **0.38\* [0.2-0.9]** | 0.49 [0.2-1.2] |
| ***Mother's HIV status*** |  |  |  |
| Negative | 1 | 1 | 1 |
| Positive pregnancy | 0.80 [0.5-1.3] | **0.56\* [0.2-0.9]** | **0.56\* [0.3-1.0]** |
| Positive since pregnancy | 0.73 [0.4-1.3] | 0.73 [0.4-1.3] | 0.73 [0.4-1.4] |
| ***Residence (at birth)*** |  |   |  |
| Rural  | 1 | 1 | 1 |
| Urban  | 1.49 [0.9-2.4] | **1.61\* [1.0-2.6]** | **2.00\*\* [1.2-3.2]** |
| ***Income provider (at birth)*** |  |  |  |
| Other | 1 | 1 | 1 |
| Mother | 0.72 [0.3-1.6] | 1.55 [0.7-3.6] | 1.22 [0.5-2.8] |
| ***Owns fridge (at birth)*** |  |  |  |
| Fridge No | 1 | 1 | 1 |
| Fridge Yes | 0.99 [0.6-1.5] | 1.21 [0.8-1.9] | 1.04 [0.7-1.7] |
| ***Perception wealth(Current)*** |  |  |  |
| Very comfortable | 1 | 1  | 1 |
| Getting by | 0.70 [0.3-1.5] | 1.36 [0.7-2.8] | 0.57 [0.3-1.2] |
| Extremely poor | 1.16 [0.5-2.6] | 2.11 [0.9-4.7] | 0.83 [0.4-1.9] |
| ***Creche*** |  |  |  |
| No creche | 1 | 1 | 1 |
| Attended creche | 3.78 [1.0-14.8] | 1.40 [0.5-4.0] | 1.84 [0.5-6.5] |
| ***MC-Homeb(Current)*** |  |  |  |
| Low Total | 1 | 1 | 1 |
| High Total | 1.30 [0.8-2.0] | 1.05 [0.7-1.6] | 1.17 [0.7-1.8] |
| ***Maternal mental health(Current)*** |  |  |  |
| No mental disorders | 1 | 1 | 1 |
| Depression or anxiety or alcohol use | **3.24\*\* [1.3-7.8]** | **2.98\*\* [1.3-6.7]** | **3.28\*\* [1.4-8.0]** |
| ***Parenting stress(Current)*** |  |  |  |
| Parenting stress ≤ 90 | 1 | 1 | 1 |
| Parenting stress ≥ 90 | **3.25\*\* [1.5-6.9]** | **2.44\* [1.2-5.2]** | **4.63\*\*\* [2.1-10.1]** |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the Confidence Intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*AORs based on multivariate logistic regression on the outcomes including all covariates. The Child Behaviour Check List (CBCL) includes 120-items in two subscales: ‘Internalising disorders’ and ‘Externalising disorders’, and a composite Total score. A high score indicates more problems.*

Table 9 Boys: Factors associated with children's emotional and behavioural outcomes measured by the Child Behaviour Checklist (CBCL)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **CBCL Internalising** | **CBCL externalising** | **CBCL total** |
|  | AOR [CI]  | AOR [CI] | AOR [CI]  |
| ***Child Age (Current)*** |  |  |  |
| 8 years | 1.00 | 1.00 | 1.00 |
| 9 years | 0.30 [0.1-1.2] | 0.76 [0.2-2.5] | 0.64 [0.2-2.1] |
| 10 years | **0.26\* [0.1-1.0]** | 0.62 [0.2-2.1] | 0.56 [0.2-1.8] |
| 11 years | 0.37 [0.1-1.7] | 0.99 [0.2-4.1] | 1.07 [0.3-4.4] |
| ***Mother's Age (at birth)*** |  |  |  |
| Less than 20 years | 1.00 | 1.00 | 1.00 |
| 20-29 years | 0.93 [0.5-1.8] | 0.82 [0.4-1.6] | 1.25 [0.6-2.4] |
| 30+ years | 0.66 [0.3-1.6] | 0.52 [0.2-1.3] | 1.11 [0.4-2.8] |
| ***Maternal IQ (Current)a*** |  |  |  |
| Low Raven’s | 1.00 | 1.00 | 1.00 |
| High Raven’s | 1.21 [0.8-1.9] | 1.07 [0.7-1.8] | 1.36 [0.8-2.2] |
| ***Mother's Education (at birth)*** |  |  |  |
| None | 1.00 | 1.00 | 1.00 |
| Primary | 0.73 [0.3-1.8] | 0.63 [0.2-1.6] | **0.30\* [0.1-0.8]** |
| Some secondary | 0.82 [0.3-2.2] | 0.60 [0.2-1.7] | **0.26\* [0.1-0.7]** |
| Completed secondary/post | 0.82 [0.3-2.4] | 0.42 [0.1-1.2] | **0.21\*\* [0.1-0.6]** |
| ***Birthweight*** |  |  |  |
| Low Birthweight | 1.00 | 1.00 | 1.00 |
| Normal Birthweight | 0.93 [0.4-2.0] | 1.06 [0.5-2.3] | 1.21 [0.6-2.6] |
| ***Exclusive Breastfeeding*** |  |  |  |
| 0-1 months | 1.00 | 1.00 | 1.00 |
| 2-5 months | 0.84 [0.4-1.8] | **0.48\* [0.2-1.0]** | 0.66 [0.3-1.4] |
| 6 months | 0.68 [0.3-1.3] | 0.56 [0.3-1.1] | 0.63 [0.3-1.3] |
| ***Birth order (Birth)*** |  |  |  |
| Birth order 1-2 | 1.00 | 1.00 | 1.00 |
| Birth order 3-4 | 1.06 [0.6-2.0] | 1.10 [0.6-2.1] | 0.81 [0.4-1.5] |
| Birth order 5+ | 0.83 [0.4-2.0] | 1.36 [0.6-3.3] | 0.62 [0.3-1.4] |
| ***Mother's HIV status*** |  |  |  |
| Negative | 1.00 | 1.00 | 1.00 |
| Positive pregnancy | 0.94 [0.6-1.5] | 1.10 [0.6-1.9] | 1.15 [0.7-2.0] |
| Positive since pregnancy | 1.28 [0.7-2.4] | 1.09 [0.6-2.1] | 1.13 [0.6-2.2] |
| ***Residence (at birth)*** |  |  |  |
| Rural  | 1.00 | 1.00 | 1.00  |
| Urban  | 1.40 [0.9-2.3] | 1.18 [0.7-1.9] | 1.31 [0.8-2.1] |
| ***Income provider (at birth)*** |  |  |  |
| Other | 1.00 | 1.00 | 1.00 |
| Mother | 1.55 [0.7-3.3] | 1.07 [0.5-2.4] | 1.75 [0.8-3.8] |
| ***Owns fridge (at birth)*** |  |  |  |
| Fridge No | 1.00 | 1.00 | 1.00 |
| Fridge Yes | 1.30 [0.8-2.1] | 0.93 [0.6-1.5] | 0.98 [0.6-1.6] |
| ***Perception wealth(Current)*** |  |  |  |
| Very comfortable | 1.00 | 1.00 | 1.00 |
| Getting by | 1.78 [0.8-4.2] | 1.06 [0.5-2.3] | 0.96 [0.4-2.1] |
| Extremely poor | 1.65 [0.7-4.2] | 0.81 [0.3-1.9] | 0.82 [0.3-1.9] |
| ***Creche*** |  |  |  |
| No creche | 1.00 | 1.00 | 1.00 |
| Attended creche | 0.63 [0.3-1.3] | **2.55\* [1.2-5.2]** | 2.14 [1.0-4.7] |
| ***MC-Homeb(Current)*** |  |  |  |
| Low Total | 1.00 | 1.00 | 1.00 |
| High Total | 1.26 [0.8-2.0] | 1.19 [0.8-1.9] | 1.36 [0.9-2.1] |
| ***Maternal mental health(Current)*** |  |  |  |
| No mental disorders | 1.00 | 1.00 | 1.00 |
| Depression or anxiety or alcohol use | 1.48 [0.7-3.4] | 1.31 [0.6-3.0] | **2.63\* [1.0-7.0]** |
| ***Parenting stress(Current)*** |  |  |  |
| Parenting stress ≤ 90 | 1.00 | 1.00 | 1.00 |
| Parenting stress ≥ 90 | **3.46\*\*\* [1.8-6.6]** | **10.35\*\*\* [4.9-21.9]** | **9.72\*\*\* [4.6-20.6]** |

Footnotes

*a High/low based on splitting the sample on the median*

*b High/low based on splitting the sample on the median*

*When the association was significant the OR and aOR are in bold (due to rounding the Confidence Intervals sometimes overlap with 1.0)*

*\* p ≤ 0.05; \*\* p < 0.01; \*\*\* p < 0.001.*

*AORs based on multivariate logistic regression on the outcomes including all covariates. The Child Behaviour Check List (CBCL) includes 120-items in two subscales: ‘Internalising disorders’ and ‘Externalising disorders’, and a composite Total score. A high score indicates more problems.*

**Discussion**

To our knowledge this is the first study examining EBF, HIV-exposure and child cognition, executive function and emotional-behavioural outcomes, at primary school age in Africa.

Our finding that duration of EBF was associated with fewer conduct disorders has significant implications. Conduct disorders lead to aggressive or disruptive behaviours which interfere with learning and peer relationships, in turn leading to low self-esteem and further behavioural problems (39). Conduct disorders in childhood are associated with an increase in violent criminal behaviour, poor long-term mental health and academic achievement in later life (40). While to our knowledge there have been no formal analyses of the economic costs of conduct disorders in Low-Middle-Income Countries, the evidence from carefully conducted studies in High-Income countries is that the costs are enormous (41). For example, a report from the UK stated that the total cost of crime attributable to people who had a conduct disorder in childhood was estimated to be £60 billion per annum (42). Given these costs to individuals, families and society, it is highly relevant that this study has shown EBF to be associated with reduced likelihood of conduct disorders at this critical stage of development. Further, for boys, a longer EBF duration was weakly associated with a doubling of the odds of better cognitive development on the Learning sub-scale which assesses ability for maintaining focused attention, while coding and storing complex auditory and visual stimuli simultaneously, and generating strategies to learn efficiently. Identifying potential strategies to improve the life chances of boys is important and, in our context, EBF appears to be associated with a longer term advantage for boys. There is increasing evidence that some groups of children are more susceptible to the effects of negative rearing and, importantly, that they may benefit more from the effects of positive rearing and interventions. This is known as the ‘differential susceptibility hypothesis’ (42). Boys may be more susceptible in a number of domains of development to the effects of negative rearing, for example in language development (43, 44) and therefore, in line with our findings, may benefit more from early EBF.

The finding that EBF did not have an effect on children’s cognitive development overall is in accord with studies from other resource-limited settings which also found no association(4), including India (n=514, aged 9-10 years), China (n=442, aged 3 years), Malaysia (n=1394, aged 9 years), Chile (n=784, aged 5.5 years), and the Philippines (n=1984, aged 8.5 and 11.5 years), although these studies did not stratify by sex.

An important strength of this study is the investigation of a wide range of key determinants of child development. In our cohort, maternal cognitive ability was strongly positively associated with children’s performance across all cognitive sub-scales, but not with executive function, although higher maternal cognitive ability was associated with improved performance on the Planning subscale, which assesses ability to focus attention, make decisions and apply working memory, abilities considered to reflect executive function(27). Interestingly, while having attended a crèche was associated with improvement in children’s cognitive development (sequential scores which depend on practice, on which boys scored particularly low) at primary school age, it was independently associated with poorer behaviour, with similar associations found for children born in urban and rural settings. This apparent paradox in relation to crèche exposure is consistent with data from high income countries (45).

Executive function is a high order cognitive function which coordinates and controls information processing (18). It is critical in enabling a child to successfully integrate into environments such as school (46). We found a positive association between executive function and better stimulation at home, older maternal age, and a mother who was the main income provider at the time of the child’s birth. These findings are in accord with evidence suggesting that executive function is susceptible to environmental factors (47). Executive function is increasingly thought of as the core ingredients (creativity, flexibility, self-control and discipline) that will determine a child’s success in life. There is evidence that executive function is negatively affected by stress, emotions, poor physical fitness and childhood obesity (39). Encouragingly, a growing body of evidence suggests that simple, low cost, interventions such as non-computerized games, aerobics, martial arts and mindfulness may support improvements in executive function (19).

Our finding that poor maternal mental health and high parenting stress, measured at the time of the child assessments, were associated with increased emotional-behavioural problems in children was unsurprising, but useful to quantify in an African setting. The link between parental mental health and child behaviour outcomes is well-established, with children of depressed, anxious or highly stressed mothers known to be at increased risk of psychological and behavioural problems (48, 49).

There is a dearth of evidence examining the developmental trajectories of HIV-exposed children, in particular longitudinal studies including HIV-unexposed controls. A recent systematic review (26) examining HIV-exposure and child development found only 11 studies (1591 children aged 0-18 years), and showed that HIV-exposed children are disadvantaged compared to their HIV-unexposed peers, in particular in emotional-behavioural, and to a lesser extent, cognitive development. However, results are not consistent across research settings or age groups, with most of the current evidence being based on small samples with wide heterogeneity in outcomes measures (26). Our results, based on a large sample of children including HIV-unexposed controls suggest that, overall, HIV-exposed children performed as well as HIV-unexposed children in the domains examined, and that the findings of other small studies may be overstated.

Limitations include the non-randomised study design of the original intervention, the lack of maternal mental health measurement at the child’s birth, and no assessment of cognition or emotional/behavioural problems at earlier time-points in the children’s lives. Infections of the developing brain and childhood malnutrition also affect later cognitive ability but were not included in the analyses. In addition, caution must be taken in interpreting the sex-stratified models, as examining sub-group effects increases uncertainty and is more likely to produce larger effect estimates. Further, due to the complexities in measuring cognitive and executive function, and the need to model each of the outcomes separately, multiple tests were used, and there may be some false positive significant results. However, our results are in line with findings from other studies.

Strengths include a large cohort of HIV-exposed and unexposed children, population normal values, adjustment for a wide range of confounders including current maternal IQ, and a battery of culturally-appropriate developmental assessments including executive function and behavioural outcomes. A unique strength in this study is the accurate documentation of daily EBF data. Both HIV-positive and HIV-negative women had high rates of EBF, with few breast health problems, likely due to the quality of lay breastfeeding counselling(25, 50). Given that all women received intensive support it is possible that this may have limited our ability to detect differences between EBF and non-EBF children.

In conclusion while EBF was not significantly associated with cognitive development at primary-school age, there was an association between EBF and a reduction in conduct disorders and, for boys, weak evidence of positive associations both in aspects of cognitive development and behavioural problems more generally. Given the number of adverse factors in these families’ environments, including poverty and high HIV prevalence, the fact that these benefits were evident into the crucial early school years is important. Child outcomes were associated with a range of other key factors. While core cognitive development was principally associated with maternal cognitive abilities, executive function was associated with a number of modifiable environmental factors including home stimulation and crèche attendance. Child’s emotional development was largely associated with caregiver mental health. These findings highlight a number of avenues for potential interventions.

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**Supporting Information**

**S1 Table:** Factors associated with children's cognitive and executive function *continuous* outcomes measured by the Kauffman Assessment Battery (KABC-II) and Developmental Neuropsychological Assessment (NEPSY)

**S2 Strobe Document**

**S3 Author Summary**